The full length clone shown in Figure 189 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 54-56 and ending at the stop codon found at nucleotide positions 909-911 (Figure 189; SEQ ID NO:271). The predicted polypeptide precursor (Figure 190, SEQ ID NO:272) is 285 amino acids long. PRO1360 has a calculated molecular weight of approximately 31,433 daltons and an estimated pI of approximately 7.32. Clone DNA59488-1603 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203157.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 190 (SEQ ID NO:272), revealed sequence identity between the PRO1360 amino acid sequence and the following Dayhoff sequences: UN51_CAEEL, YD4B_SCHPO, AF000634_1, GFO_ZYMMO, YEIJ_SCHPO, D86566_1, ZMGFO_1, S76976, PPSA_SYNY3, and CEF28B1_4.

EXAMPLE 84: Isolation of cDNA clones Encoding Human PRO1029

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 18763. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57854.

In light of an observed sequence homology between the DNA57854 conscnsus sequence and an EST sequence encompassed within the Merck EST clone no. T98880, the Merck EST clone T98880 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 191 and is herein designated as DNA59493-1420.

Clone DNA59493-1420 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 39-41 and ending at the stop codon at nucleotide positions 297-299 (Figure 191). The predicted polypeptide precursor is 86 amino acids long (Figure 192). The full-length PRO1029 protein shown in Figure 192 has an estimated molecular weight of about 9,548 daltons and a pI of about 8.52. Analysis of the full-length PRO1029 sequence shown in Figure 192 (SEQ ID NO:274) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, an amino acid block having homology to bacterial rhodopsins retinal binding site protein from about amino acid 50 to about amino acid 61, a prenyl group binding site from about amino acid 83 to about amino acid 86 and a potential N-glycosylation site from about amino acid 45 to about amino acid 48. Clone DNA59493-1420 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203050,

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 192 (SEQ ID NO:274), evidenced significant

homology between the PRO1029 amino acid sequence and the following Dayhoff sequences: S66088, AF031815_1, MM4A6L_1, PSEIS52a-1, S17699 and P_R63635.

EXAMPLE 85: Isolation of cDNA clones Encoding Human PRO1139

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 4461. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57312.

The DNA57312 consensus sequence included a 172 nucleotides long public EST (T62095, Merck/University of Washington public database). This EST clone, identified herein as a putative protein coding sequence, was purchased from Merck, and sequenced to provide the coding sequence of PRO1139 (Figure 193). As noted before, the deduced amino acid sequence of DNA59497-1496 shows a significant sequence identity with the deduced amino acid sequence of HSOBRGRP_1. The full-length protein (Figure 194) contains a putative signal peptide between amino acid residues 1 and about 28, and three putative transmembrane domains (approximate amino acid residues 33-52, 71-89, 98-120).

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EXAMPLE 86: Isolation of cDNA clones Encoding Human PRO1309

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to SLIT.

RNA for construction of cDNA libraries was isolated from human fetall brain tissue. The cDNA libraries used to isolate the cDNA clones encoding human PRO1309 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe derived from the above described Incyte EST sequence:

5'-TCCGTGCAGGGGGACGCCTTTCAGAAACTGCGCCGAGTTAAGGAAC-3' (SEQ ID NO:279).

A cDNA clone was isolated and sequenced in entirety. The entire nucleotide sequence of DNA59588-1571 is shown in Figure 195 (SEQ ID NO:277). Clone DNA59588-1571 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 720-722 and a stop codon at nucleotide positions 2286-2288 (Figure 195; SEQ ID NO:277). The predicted polypeptide precursor is 522 amino acids

long. The signal peptide is approximately at 1-34 and the transmembrane domain is at approximately 428-450 of SEQ ID NO:278. Clone DNA59588-1571 has been deposited with ATCC and is assigned ATCC deposit no. 203106. The full-length PRO1309 protein shown in Figure 196 has an estimated molecular weight of about 58,614 daltons and a pI of about 7.42.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 196 (SEQ ID NO:278), revealed sequence identity between the PRO1309 amino acid sequence and the following Dayhoff sequences: AB007876_1, GPV_MOUSE, ALS_RAT, P_R85889, LUM_CHICK, AB014462_1, PGS1_CANFA, CEM88_7, A58532 and GEN11209.

EXAMPLE 87: Isolation of cDNA Clones Encoding Human PRO1028

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA59603.

In light of an observed sequence homology between the DNA59603 sequence and an EST sequence contained within Incyte EST clone no. 1497725, the Incyte EST clone no. 1497725 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 197 and is herein designated as DNA59603-1419.

The entire nucleotide sequence of DNA59603-1419 is shown in Figure 197 (SEQ ID NO:280). Clone DNA59603-1419 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 21-23 and ending at the stop codon at nucleotide positions 612-614 (Figure 197). The predicted polypeptide precursor is 197 amino acids long (Figure 198). The full-length PRO1028 protein shown in Figure 198 has an estimated molecular weight of about 20,832 daltons and a pl of about 8.74. Clone DNA59603-1419 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:281, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:281. An N-glycosylation site is at about amino acids 35-38 of SEQ ID NO:281. A C-type lectin domain is at about amino acids 108-117 of SEQ ID NO:281, indicating that PRO513 may be related to or be a lectin. The corresponding nucleotides of these amino acid sequences or others can be routinely determined given the sequences provided herein.

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EXAMPLE 88: Isolation of cDNA Clones Encoding Human PRO1027

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Use f the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56399.

In light of an observed sequence homology between the DNA56399 sequence and an EST sequence contained within Incyte EST clone no. 937605, the Incyte EST clone no. 937605 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 199 and is herein designated as DNA59605-1418.

The entire nucleotide sequence of DNA59605-1418 is shown in Figure 199 (SEQ ID NO:282). Clone DNA59605-1418 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 262-264 (Figure 199). The predicted polypeptide precursor is 77 amino acids long (Figure 200). The full-length PRO1027 protein shown in Figure 200 has an estimated molecular weight of about 8,772 daltons and a pI of about 9.62. Clone DNA59605-1418 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:283, the putative signal peptide is at about amino acids 1-33 of SEQ ID NO:283. The type II fibronectin collagen-binding domain begins at about amino acid 30 of SEQ ID NO:283. The corresponding nucleotides for these amino acid sequences and others can be routinely determined given the sequences provided herein. PRO1027 may be involved in tissue formation or repair.

The following Dayhoff designations appear to have some sequence identity with PRO1027: SFT2_YEAST; ATM3E9_2; A69826; YM16_MARPO; E64896; U60193_2; MTLRAJ205_1; MCU60315_70; SPAS_SHIFL; and S54213.

EXAMPLE 89: Isolation of cDNA Clones Encoding Human PRO1107

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA56402.

In light of an observed sequence homology between the DNA56402 sequence and an EST sequence contained within Incyte EST clone no. 3203694, the Incyte EST clone no. 3203694 was purchased and the cDNA insert was brained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 201 and is herein designated as DNA59606-1471.

The entire nucleotide sequence of DNA59606-1471 is shown in Figure 201 (SEQ ID NO:284). Clone DNA59606-1471 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 244-246 and ending at the stop codon at nucleotide positions 1675-1677 of SEQ ID NO:284 (Figure 201). The predicted polypeptide precursor is 477 amino acids long (Figure 202). The full-length PRO1107 protein shown in Figure 202 has an estimated molecular weight of about 54,668 daltons and a pI of about 6.33. Clone DNA59606-1471 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1107 polypeptide suggests that it possesses significant sequence similarity to phosphodiesterase I/nucleotide phyrophosphatase, human insulin receptor tyrosine kinase inhibitor, alkaline phosphodiesterase and autotaxin, thereby indicating that PRO1107 may have at least one or all of the activities of these proteins, and that PRO1107 is a novel phosphodiesterase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1107 amino acid sequence and at least the following Dayhoff sequences: AF005632_1, P_R79148, RNU78787_1, AF060218_4, A57080 and HUMATXT_1.

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EXAMPLE 90: Isolation of cDNA clones Encoding Human PRO1140

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence No. 135917. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56416.

In light of an observed sequence homology between DNA56416 and an EST sequence contained within Incyte EST clone no. 3345705, Incyte EST clone no. 3345705 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein The sequence, designated herein as DNA59607-1497, which is shown in Figure 203, is the full-length DNA sequence for PRO1140. Clone DNA59607-1497 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

The entire nucleotide sequence of DNA59607-1497 is shown in Figure 203 (SEQ ID NO:286). Clone DNA59607-1497 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 210-212 and ending at the stop codon at nucleotide positions 975-977 (Figure 203). The predicted polypeptide precursor is 255 amino acids long (Figure 204). The full-length PRO1140 protein shown in Figure 204 has an estimated molecular weight of about 29,405 daltons and a pI of about 7.64. Analysis of the full-length PRO1140 sequence shown in Figure 204 (SEQ ID NO:287) evidences the presence of three transmembrane domains at about amino acids 101 to 118, 141 to 161 and 172 to 191.

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Analysis of the amino acid sequence of the full-length PRO1140 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1140 amino acid sequence and the following Dayhoff sequences: AF023602_1, AF000368_1, CIN3_RAT, AF0003373_1, GEN13279, and AF0003372_1.

Clone DNA59607-1497 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

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EXAMPLE 91: Isolation of cDNA clones Encoding Human PRO1106

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[™], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56423.

In light of an observed sequence homology between DNA56423 and an EST sequence contained within Incyte EST clone no. 1711247, Incyte EST clone no. 1711247 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein The sequence, designated herein as DNA59609-1470, which is shown in Figure 205, is the full-length DNA sequence for PRO1106. Clone DNA59609-1470 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209963.

The entire nucleotide sequence of DNA59609-1470 is shown in Figure 205 (SEQ ID NO:288). Clone DNA59609-1470 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 1468-1470 of SEQ ID NO:288 (Figure 205). The predicted polypeptide precursor is 469 amino acids long (Figure 206). The full-length PRO1106 protein shown in Figure 206 has an estimated molecular weight of about 52,689 daltons and a pI of about 8.68. It is understood that the skilled artisan can construct the polypeptide or nucleic acid encoding therefor to exclude any one or more of all of these domains. For example, the transmembrane domain region(s) and/or either of the amino terminal or carboxyl end can be excluded. Clone DNA59609-1470 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1106 polypeptide suggests that it possesses significant sequence similarity to the peroxisomal ca-dependent solute carrier, thereby indicating that PRO1106

may be a n vel transporter. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1106 amino acid sequence and at least the following Dayhoff sequences, AF004161_1, IG002N01_25, GDC_BOVIN and BT1_MAIZE.

EXAMPLE 92: Isolation of cDNA clones Encoding Human PRO1291

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 120480. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56425.

In light of an observed sequence homology between the DNA56425 sequence and an EST sequence encompassed within the Incyte EST clone no. 2798803, the Incyte EST clone 2798803 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 207 and is herein designated as DNA59610-1556.

Clone DNA59610-1556 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 907-909 (Figure 207). The predicted polypeptide precursor is 282 amino acids long (Figure 208). The full-length PRO1291 protein shown in Figure 208 has an estimated molecular weight of about 30,878 daltons and a pI of about 5.27. Analysis of the full-length PRO1291 sequence shown in Figure 208 (SEQ ID NO:291) evidences the presence of the following: a signal peptide from about amino acid I to about amino acid 28, a transmembrane domain from about amino acid 258 to about amino acid 281 and potential N-glycosylation sites from about amino acid 112 to about amino acid 115, from about amino acid 160 to about amino acid 163, from about amino acid 190 to about amino acid 193, from about amino acid 216 to about amino acid 219 and from about amino acid 220 to about amino acid 223.. Clone DNA59610-1556 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209990.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 208 (SEQ ID NO:291), evidenced significant homology between the PRO1291 amino acid sequence and the following Dayhoff sequences: HSU90552_1, HSU90144_1, AF033107_1, HSB73_1, HSU90142_1, GGCD80_1, P_W34452, MOG_MOUSE, B39371 and P_R71360.

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EXAMPLE 93: Isolation of cDNA clones Encoding Human PRO1105

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56430.

In light of an observed sequence homology between the DNA56430 sequence and an EST sequence encompassed within the Incyte EST clone no. 1853047, the Incyte EST clone 1853047 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 209 and is herein designated as DNA59612-1466.

The entire nucleotide sequence of DNA59612-1466 is shown in Figure 209 (SEQ ID NO:292). Clone DNA59612-1466 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 28-30 and ending at the stop codon at nucleotide positions 568-570 of SEQ ID NO:292 (Figure 209). The predicted polypeptide precursor is 180 amino acids long (Figure 210). The full-length PRO1105 protein shown in Figure 210 has an estimated molecular weight of about 20,040 daltons and a pI of about 8.35. Clone DNA59612-1466 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 210, a signal peptide is at about amino acids 1-19 of SEQ ID NO:293 and transmembrane domains are shown at about amino acids 80-99 and 145-162 of SEQ ID NO:293. It is understood that the skilled artisan could form a polypeptide with all of or any combination or individual selection of these regions. It is also understood that the corresponding nucleic acids can be routinely identified and prepared based on the information provided herein.

EXAMPLE 94: Isolation of cDNA clones Encoding Human PRO511

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the pr gram "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56434.

In light f an observed sequence homology between the DNA56434 sequence and an EST sequence encompassed within the Incyte EST clone no. 1227491, the Incyte EST clone 1227491 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 211 and is herein designated as DNA59613-1417.

The entire nucleotide sequence of DNA59613-1417 is shown in Figure 211 (SEQ ID NO:294). Clone DNA59613-1417 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 233-235 and ending at the stop codon at nucleotide positions 944-946 (Figure 211). The predicted polypeptide precursor is 237 amino acids long (Figure 212). The full-length PRO511 protein shown in Figure 212 has an estimated molecular weight of about 25,284 daltons and a pl of about 5.74. Clone DNA59613-1417 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:295, the putative signal peptide is at about amino acids 1-25 of SEQ ID NO:295. The N-glycosylation sites are at about amino acids 45-48, 73-76, 107-110, 118-121, 132-135, 172-175, 175-178 and 185-188 of SEQ ID NO:295. An arthropod defensins conserved region is at about amino acids 176-182 of SEQ ID NO:295. A kringle domain begins at about amino acid 128 of SEQ ID NO:295 and a ly-6/u-PAR domain begins at about amino acid 6 of SEQ ID NO:295. The corresponding nucleotides of these amino acid sequences and others can be routinely determined given the sequences provided herein.

The designations appearing in a Dayhoff database with which PRO511 has some sequence identity are as follows: SSC20F10_1; SF041083; P_W26579; S44208; JC2394; PSTA_DICDI; A27020; S59310; RAG1_RABIT; and MUSBALBC1_1.

EXAMPLE 95: Isolation of cDNA clones Encoding Human PRO1104

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of 25 expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56446.

In light of an observed sequence homology between the DNA56446 sequence and an EST sequence encompassed within the Incyte EST clone no. 2837496, the Incyte EST clone 2837496 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 213 and is herein designated as DNA59616-1465.

The entire nucleotide sequence of DNA59616-1465 is shown in Figure 213 (SEQ ID NO:296). Clone DNA59616-1465 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 109-111 and ending at the stop codon at nucleotide positions 1132-1134 of SEQ ID NO:296 (Figure 213). The predicted polypeptide precursor is 341 amino acids long (Figure 214). The full-length PRO1104 protein shown in Figure 214 has an estimated molecular weight of about 36,769 daltons and a pI of about 9.03. Clone DNA59616-1465 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 214, a signal peptide is at about amino acids 1-22 of SEQ ID NO:297. N-myristoylation sites are at about amino acids 41-46, 110-115, 133-138, 167-172 and 179-184 of SEQ ID NO:297.

10 EXAMPLE 96: Isolation of cDNA clones Encoding Human PRO1100

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the obtained consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2305379, the Incyte EST clone 2305379 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 215 and is herein designated as DNA59619-1464.

The entire nucleotide sequence of DNA59619-1464 is shown in Figure 215 (SEQ ID NO:298). Clone DNA59619-1464 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 33-35 and ending at the stop codon at nucleotide positions 993-995 of SEQ ID NO:298 (Figure 215). The predicted polypeptide precursor is 320 amino acids long (Figure 216). The full-length PRO1100 protein shown in Figure 216 has an estimated molecular weight of about 36,475 daltons and a pI of about 7.29. Clone DNA59619-1464 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Upon analyzing SEQ ID NO:299, the approximate locations of the signal peptide, the transmembrane domains, an N-glycosylation site, an N-myristoylation site, a CUB domain and an amiloride-sensitive sodium channel domain are present. It is believed that PRO1100 may function as a channel. The corresponding nucleic acids for these amino acids and others can be routinely determined given SEQ ID NO:299...

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EXAMPLE 97: Isolation of cDNA clones Encoding Human PRO836

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is herein designated DNA56453.

In light of an observed sequence homology between the DNA56453 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2610075, the Incyte EST clone 2610075 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 217 and is herein designated as DNA59620-1463.

The entire nucleotide sequence of DNA59620-1463 is shown in Figure 217 (SEQ ID NO:300). Clone DNA59620-1463 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 65-67 and ending at the stop codon at nucleotide positions 1448-1450 of SEQ ID NO:300 (Figure 217). The predicted polypeptide precursor is 461 amino acids long (Figure 218). The full-length PRO836 protein shown in Figure 218 has an estimated molecular weight of about 52,085 daltons and a pI of about 5.36. Analysis of the full-length PRO836 sequence shown in Figure 218 (SEQ ID NO:301) evidences the presence of the following: a signal peptide, N-glycosylation sites, N-myristoylation sites, a domain conserved in the YJL126w/YLR351c/yhcX family of proteins, and a region having sequence identity with SLS1. Clone DNA59620-1463 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO836 polypeptide suggests that it possesses some sequence similarity to SLS1, thereby indicating that PRO836 may be involved in protein translocation of the ER. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some homology between the PRO836 amino acid sequence and at least the following Dayhoff sequences, S58132, SPBC3B9_1, S66714, CRU40057 1 and IMA CAEEL.

EXAMPLE 98: Isolation of cDNA clones Encoding Human PRO1141

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 11873. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or

in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56518.

In light of an observed sequence homology between the DNA56518 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2679995, the Incyte EST clone 2679995 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 219 and is herein designated as DNA59625-1498.

Clone DNA59625-1498 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 204-206 and ending at the stop codon at nucleotide positions 945-947 (Figure 219). The predicted polypeptide precursor is 247 amino acids long (Figure 220). The full-length PRO1141 protein shown in Figure 220 has an estimated molecular weight of about 26,840 daltons and a pI of about 8.19. Analysis of the full-length PRO1141 sequence shown in Figure 220 (SEQ ID NO:303) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and transmembrane domains from about amino acid 38 to about amino acid 57, from about amino acid 67 to about amino acid 83, from about amino acid 117 to about amino acid 139 and from about amino acid 153 to about amino acid 170. Clone DNA59625-1498 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209992.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 220 (SEQ ID NO:303), evidenced significant homology between the PRO1141 amino acid sequence and the following Dayhoff sequences: CEVF36H2L_2, PCRB7PRJ_1, AB000506_1, LEU95008_1, MRU87980_15, YIGM_ECOLI, STU65700_1, GHU62778_1, CYST SYNY3 and AF009567 1.

EXAMPLE 99: Isolation of cDNA clones Encoding Human PRO1132

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A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35934. Based on the DNA35934 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1132.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-TCCTGTGACCACCCCTCTAACACC-3' (SEQ ID NO:310) and

30 reverse PCR primer: 5'-CTGGAACATCTGCTGCCCAGATTC-3' (SEQ ID NO:311).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus sequence which had the following nucleotide sequence:

5'-GTCGGATGACAGCAGCAGCCGCATCATCAATGGATCCGACTGCGATATGC-3' (SEQ ID NO:312).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1132 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1132 and the derived protein sequence for PRO1132.

The entire nucleotide sequence of PRO1132 is shown in Figure 225 (SEQ ID NO:308). Clone DNA59767-1489 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 354-356 and a stop codon at nucleotide positions 1233-1235 (Figure 225; SEQ ID NO:308). The predicted polypeptide precursor is 293 amino acids long. The signal peptide is at about amino acids 1-22 and the histidine active site is at about amino acids 104-109 of SEQ ID NO:309. Clone DNA59767-1489 has been deposited with ATCC (having the actual sequence rather than representations based on sequencing techniques as presented herein) and is assigned ATCC deposit no. 203108. The full-length PRO1132 protein shown in Figure 226 has an estimated molecular weight of about 32,020 daltons and a pl of about 8.7.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 226 (SEQ ID NO:309), revealed sequence identity between the PRO1132 amino acid sequence and the following Dayhoff sequences: SSU76256_1, P_W10694, MMAE000663_6, AF013988_1, U66061_8, MMAE000665_2, MMAE00066415, MMAE00066414, MMAE000665_4 and MMAE00066412.

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EXAMPLE 100: Isolation of cDNA clones Encoding Human NL7 (PRO1346)

A single EST sequence (#1398422) was found in the LIFESEQ^{*} database as described in Example 1 above. This EST sequence was renamed as DNA45668. Based on the DNA45668 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for NL7.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CACACGTCCAACCTCAATGGGCAG-3' (SEQ ID NO:315)

reverse PCR primer: 5'-GACCAGCAGGGCCAAGGACAAGG-3' (SEQ ID NO:316)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus

DNA45668 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GTTCTCTGAGATGAAGATCCGGCCGGTCCGGGAGTACCGCTTAG-3' (SEQ ID NO:317)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the NL7 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human fetal kidney library (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for NL7 (designated herein as DNA59776-1600 [Figure 227, SEQ ID NO:313]) and the derived protein sequence for NL7 (PRO1346).

The entire coding sequence of NL7 (PRO1346) is shown in Figure 227 (SEQ ID NO:313). Clone DNA59776-1600 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 1-3 and an apparent stop codon at nucleotide positions 1384-1386. The predicted polypeptide precursor is 461 amino acids long. The protein contains an apparent type II transmembrane domain at amino acid positions from about 31 t about 50; fibrinogen beta and gamma chains C-terminal domain signature starting at about amino acid position 409, and a leucine zipper pattern starting at about amino acid positions 140, 147, 154 and 161, respectively. Clone DNA59776-1600 has been deposited with ATCC and is assigned ATCC deposit no. 203128. The full-length NL7 protein shown in Figure 228 has an estimated molecular weight of about 50,744 daltons and a pI of about 6.38.

Based on a WU-BLAST2 sequence alignment analysis (using the WU-BLAST2 computer program) of the full-length sequence, NL7 shows significant amino acid sequence identity to a human microfibril-associated glycoprotein (1 MFA4_HUMAN); to known TIE-2 ligands and ligand homologues, ficolin, serum lectin and TGF-1 binding protein.

EXAMPLE 101: Isolation of cDNA clones Encoding Human PRO1131

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43546 (see Figure 231; SEQ ID NO:320). The DNA43546 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45627.

Based on the DNA45627 sequence, oligonucleotide probes were generated and used to screen a human library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., <u>Science</u> 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and 2 reverse) were synthesized:

forward PCR primer 5'-ATGCAGGCCAAGTACAGCAGCAC-3' (SEQ ID NO:321); reverse PCR primer 1 5'-CATGCTGACGACTTCCTGCAAGC-3' (SEQ ID NO:322); and reverse PCR primer 1 5'-CCACACAGTCTCTGCTTCTTGGG-3' (SEQ ID NO:323)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45627 sequence which had the following nucleotide sequence:

hybridization probe

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5'-ATGCTGGATGATGGGGACACCACCATGAGCCTGCATT-3' (SEQ ID NO:324).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1131 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 144-146, and a stop signal at nucleotide positions 984-986 (Figure 229; SEQ ID NO:318). The predicted polypeptide precursor is 280 amino acids long, has a calculated molecular weight of approximately 31,966 daltons and an estimated pl f approximately 6.26. The transmembrane domain sequence is at about 49-74 of SEQ ID NO:319 and the region having sequence identity with LDL receptors is about 50-265 of SEQ ID NO:319. PRO1131 contains potential N-linked glycosylation sites at amino acid positions 95-98 and 169-172 of SEQ ID NO:319. Clone DNA59777-1480 has been deposited with the ATCC and is assigned ATCC deposit no. 203111.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 230 (SEQ ID NO:319), evidenced some sequence identity between the PRO1131 amino acid sequence and the following Dayhoff sequences: AB010710_1, 149053, 149115, RNU56863_1, LY4A_MOUSE, I55686, MMU56404_1, 149361, AF030313_1 and MMU09739_1.

EXAMPLE 102: Isolation of cDNA clones Encoding Human PRO1281

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35720. Based on the DNA35720 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1281.

PCR primers (forward and reverse) were synthesized:

forward PCR primers:

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- 20 5'-TGGAAGGCTGCCGCAACGACAATC-3' (SEQ ID NO:327);
 - 5'-CTGATGTGGCCGATGTTCTG-3' (SEQ ID NO:328); and
 - 5'-ATGGCTCAGTGTGCAGACAG-3' (SEQ ID NO:329).

reverse PCR primers:

- 5'-GCATGCTCCGTGAAGTAGTCC-3' (SEO ID NO:330); and
- 25 5'-ATGCATGGGAAAGAAGGCCTGCCC-3' (SEQ ID NO:331).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA35720 sequence which had the following nucleotide sequence:

hybridization probe:

- 5'-TGCACTGGTGACCACGAGGGGGTGCACTATAGCCATCTGGAGCTGAG-3' (SEQ ID NO:332).
- In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1281 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1281 (designated herein as DNA59820-1549 [Figure 232, SEQ ID NO:325]; and the derived protein sequence for PRO1281.

The entire coding sequence of PRO1281 is shown in Figure 232 (SEQ ID NO:325). Clone DNA59820-1549 contains a single pen reading frame with an apparent translational initiation site at nucleotide positions 228-230 and an apparent stop codon at nucleotide positions 2553-2555. The predicted polypeptide precursor is 775 amino acids long. The full-length PRO1281 protein shown in Figure 233 has an estimated molecular weight of about 85,481 daltons and a pI of about 6.92. Additional features include a signal peptide at about amino acids 1-15; and potential N-glycosylation sites at about amino acids 138-141 and 361-364.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 233 (SEQ ID NO:326), revealed some sequence identity between the PRO1281 amino acid sequence and the following Dayhoff sequences: S44860, CET24D1_1, CEC38H2_3, CAC2_HAECO, B3A2_HUMAN, S22373, CEF38A3_2, CEC34F6_2, CEC34F6_3, and CELT22B11_3.

Clone DNA59820-1549 has been deposited with ATCC and is assigned ATCC deposit no. 203129.

EXAMPLE 103: Isolation of cDNA clones Encoding Human PRO1064

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-BLAST2 sequence alignment computer program, to have no significant sequence identity to any known human 15 protein. This cDNA sequence is herein designated DNA45288. The DNA45288 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 20 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA48609. Oligonucleotide primers based upon the DNA48609 sequence were then synthesized and employed to screen a human fetal kidney cDNA library which resulted in the identification of the DNA59827-1426 clone shown in Figure 234. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the Sfil site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed were as follows:

forward PCR primer 5'-CTGAGACCCTGCAGCACCATCTG-3' (SEQ ID NO:336)

30 reverse PCR primer 5'-GGTGCTTCTTGAGCCCCACTTAGC-3' (SEQ ID NO:337)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA48609 sequence which had the following nucleotide sequence

hybridization probe

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5'-AATCTAGCTTCTCCAGGACTGTGGTCGCCCGTCCGCTGT-3' (SEQ ID NO:338)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 532-534 and a stop signal at nucleotide positions 991-993 (Figure 234, SEQ ID NO:333). The predicted polypeptide precursor is 153 amino acids long, has a calculated

molecular weight of approximately 17,317 daltons and an estimated pl of approximately 5.17. Analysis of the full-length PRO1064 sequence shown in Figure 235 (SEQ ID NO:334) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 89 to about amino acid 110, an indole-3-glycerol phosphate synthase homology block from about amino acid 74 to about amino acid 105 and a Myb DNA binding domain protein repeat protein homology block from about amino acid 114 to about amino acid 137. Clone DNA59827-1426 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203089.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 235 (SEQ ID NO:334), evidenced homology between the PRO1064 amino acid sequence and the following Dayhoff sequences: MMNP15PRO_1, BP187PLYH_1, CELF42G8_4, MMU58888_1, GEN14270, TUB8_SOLTU, RCN_MOUSE, HUMRBSY79_1, SESENODA 1 and A21467 1.

EXAMPLE 104: Isolation of cDNA clones Encoding Human PRO1379

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA45232. Based on the DNA45232 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1379.

PCR primers (forward and reverse) were synthesized:

20 <u>forward PCR primer</u> 5'-TGGACACCGTACCCTGGTATCTGC-3' (SEQ ID NO:341) <u>reverse PCR primer</u> 5'-CCAACTCTGAGGAGAGCAAGTGGC-3' (SEQ ID NO:342)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45232 sequence which had the following nucleotide sequence:

hybridization probe

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25 5'-TGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAAC-3' (SEQ ID NO:343).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1379 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1379 which is designated herein as DNA59828-1608 and shown in Figure 237 (SEQ ID NO:339); and the derived protein sequence for PRO1379 (SEQ ID NO:340).

The entire coding sequence of PRO1379 is shown in Figure 237 (SEQ ID NO:339). Clone DNA59828-1608 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 10-12 and an apparent stop codon at nucleotide positions 1732-1734. The predicted polypeptide precursor is 574 amino acids long. The full-length PRO1379 protein shown in Figure 238 has an estimated molecular weight of about 65,355 daltons and a pl of about 8.73. Additional features include a signal peptide at about amino acids

1-17 and potential N-glycosylation sites at about amino acids 160-163, 287-290, and 323-326.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 238 (SEQ ID NO:340), revealed some homology between the PRO1379 amino acid sequence and the following Dayhoff sequences: YHY8_YEAST, AF040625_1, HP714394_1, and HIV18U45630_1.

Clone DNA59828-1608 has been deposited with ATCC and is assigned ATCC deposit no. 203158.

EXAMPLE 105: Isolation of cDNA Clones Encoding Human PRO844

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An expressed sequence tag (EST) DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed sequence identity with aLP. Based on the information and discoveries provided herein, the clone for this EST, Incyte clone no. 2657496 from a cancerous lung library was further examined.

DNA sequencing of the insert for this clone gave a sequence (herein designated as DNA59838-1462; SEQ ID NO:344) which includes the full-length DNA sequence for PRO844 and the derived protein sequence for PRO844.

The entire nucleotide sequence of DNA59838-1462 is shown in Figure 239 (SEQ ID NO:344). Clone DNA59838-1462 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 5-7 and ending at the stop codon at nucleotide positions 338-340 of SEQ ID NO:344 (Figure 239). The predicted polypeptide precursor is 111 amino acids long (Figure 240). The full-length PRO844 protein shown in Figure 240 has an estimated molecular weight of about 12,050 daltons and a pl of about 5.45. Clone UNQ544 DNA59838-1462 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO844 polypeptide suggests that it possesses significant sequence similarity to serine protease inhibitors, thereby indicating that PRO844 may be a novel proteinase inhibitor. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO844 amino acid sequence and at least the following Dayhoff sequences, ALK1_HUMAN, P_P82403, P_P82402, ELAF_HUMAN and P_P60950.

EXAMPLE 106: Isolation of cDNA Clones Encoding Human PRO848

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA55999.

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In light of an observed sequence homology between the DNA55999 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2768571, the Incyte EST clone 2768571 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 241 and is herein designated as DNA59839-1461.

The entire nucleotide sequence of DNA59839-1461 is shown in Figure 241 (SEQ ID NO:346). Clone DNA59839-1461 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 146-148 and ending at the stop codon at nucleotide positions 1946-1948 of SEQ ID NO:346 (Figure 241). The predicted polypeptide precursor is 600 amino acids long (Figure 242). The full-length PRO848 protein shown in Figure 242 has an estimated molecular weight of about 68,536 daltons. Clone DNA59839-1461 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO848 polypeptide suggests that it may be a novel sialyltransferase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO848 amino acid sequence and at least the following Dayhoff sequences, P_R78619 (GalNAc-alpha-2, 6-sialyltransferase), CAAG5_CHICK (alpha-n-acetylgalactosamide alpha-2, 6-sialyltransferase), HSU14550_1,CAG6_HUMAN and P_R63217 (human alpha-2, 3-sialyltransferase).

EXAMPLE 107: Isolation of cDNA Clones Encoding Human PRO1097

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56006.

In light of an observed sequence homology between the DNA56006 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2408105, the Incyte EST clone 2408105 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 243 and is herein designated as DNA59841-1460.

The entire nucleotide sequence of DNA59841-1460 is shown in Figure 243 (SEQ ID NO:348). Clone DNA59841-1460 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 3-5 and ending at the stop codon at nucleotide positions 276-278 of SEQ ID NO:348 (Figure 243). The predicted polypeptide precursor is 91 amino acids long (Figure 244). The full-length PRO1097 protein shown in Figure 244 has an estimated molecular weight of about 10,542 daltons and a pI of about 10.04. Clone DNA59841-1460 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has

the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 244, the signal peptide is at about amino acids 1-20 of SEQ ID NO:349. The glycoprotease family protein domain starts at about amino acid 56, and the acyltransferase ChoActase/COT/CPT family peptide starts at about amino acid 49 of SEQ ID NO:349.

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EXAMPLE 108: Isolation of cDNA clones Encoding Human PRO1153

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ*, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56008.

In light of an observed sequence homology between the DNA56008 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2472409, the Incyte EST clone 2472409 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 245 and is herein designated as DNA59842-1502.

The full length clone shown in Figure 245 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon found at nucleotide positions 683-685 (Figure 245; SEQ ID NO:350). The predicted polypeptide precursor (Figure 246, SEQ ID NO:351) is 197 amino acids long. PRO1153 has a calculated molecular weight of approximately 21,540 daltons and an estimated pl of approximately 8.31. Clone DNA59842-1502 has been deposited with ATCC and is assigned ATCC deposit no. 209982. It is understood that the correct and actual sequence is in the deposited clone while herein are present representations based on current sequencing techniques which may have minor errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1153 shows some amino acid sequence identity to the following Dayhoff designations: S57447; SOYHRGPC_1; S46965; P_P82971; VCPHEROPH_1; EXTN_TOBAC; MLCB2548_9; ANXA_RABIT; JC5437 and SSGP_VOLCA.

EXAMPLE 109: Isolation of cDNA clones Encoding Human PRO1154

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in

Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56025.

In light of an observed sequence homology between the DNA56025 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2169375, the Incyte EST clone 2169375 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 247 and is herein designated as DNA59846-1503.

The full length clone shown in Figure 247 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86-88 and ending at the stop codon found at nucleotide positions 2909-2911 (Figure 247; SEQ ID NO:352). The predicted polypeptide precursor (Figure 248, SEQ ID NO:353) is 941 amino acids long. PRO1154 has a calculated molecular weight of approximately 107,144 daltons and an estimated pI of approximately 6.26. Clone DNA59846-1503 has been deposited with ATCC and is assigned ATCC deposit no. 209978.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1154 shows sequence identity to at least the following Dayhoff designations: AB011097_1, AMPN_HUMAN, RNU76997_1, 159331, GEN14047, HSU62768_1, P_R51281, CET07F10_1, SSU66371_1, and AMPRE_HUMAN.

EXAMPLE 110: Isolation of cDNA clones Encoding Human PRO1181

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 82468. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56029.

In light of an observed sequence homology between the DNA56029 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2186536, the Incyte EST clone 2186536 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 249 and is herein designated as DNA59847-1511.

Clone DNA59847-1511 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1328-1330 (Figure 249). The predicted polypeptide precursor is 437 amino acids long (Figure 250). The full-length PRO1181 protein shown in Figure 250 has an estimated molecular weight of about 46,363 daltons and a pl of about 6.22. Analysis of the full-length PRO1181 sequence shown in Figure 250 (SEQ ID NO:355) evidences the presence of the

following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from about amino acid 46 to about amino acid 49, from about amino acid 189 to about amino acid 192 and from about amino acid 382 to about amino acid 385 and amino acid sequence blocks having homology to Ly-6/u-PAR domain proteins from about amino acid 287 to about amino acid 300 and from about amino acid 98 to about amino acid 111. Clone DNA59847-1511 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203098.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 250 (SEQ ID NO:355), evidenced homology between the PRO1181 amino acid sequence and the following Dayhoff sequences: AF041083_1, P_W26579, RNMAGPIAN_1, CELT13C2_2, LMSAP2GN_1, S61882, CEF35C5_12, DP87_DICDI, GIU47631_1 and P R07092.

EXAMPLE 111: Isolation of cDNA clones Encoding Human PRO1182

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 146647. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56033.

In light of an observed sequence homology between the DNA56033 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2595195, the Incyte EST clone 2595195 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 251 and is herein designated as DNA59848-1512.

Clone DNA59848-1512 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 67-69 and ending at the stop codon at nucleotide positions 880-882 (Figure 251). The predicted polypeptide precursor is 271 amino acids long (Figure 252). The full-length PRO1182 protein shown in Figure 252 has an estimated molecular weight of about 28,665 daltons and a pI of about 5.33. Analysis of the full-length PRO1182 sequence shown in Figure 252 (SEQ ID NO:357) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, an amino acid block having homology to C-type lectin domain proteins from about amino acid 247 to about amino acid 256 and an amino acid sequence block having homology to C1q domain proteins from about amino acid 44 to about amino acid 77. Clone DNA59848-1512 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203088.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 252 (SEQ ID NO:357), evidenced significant

homology between the PRO1182 amino acid sequence and the following Dayhoff sequences: PSPD_BOVIN, CL43_BOVIN, CONG_BOVIN, P_W18780, P_R45005, P_R53257 and CELEGAP7_1.

EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1155

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single

5 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)

10 or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56102.

In light of an observed sequence homology between the DNA56102 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2858870, the Incyte EST clone 2858870 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 253 and is herein designated as DNA59849-1504.

The full length clone shown in Figure 253 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 158-160 and ending at the stop codon found at nucleotide positions 563-565 (Figure 253; SEQ ID NO:358). The predicted polypeptide precursor (Figure 254, SEQ ID NO:359) is 135 amino acids long. PRO1155 has a calculated molecular weight of approximately 14,833 daltons and an estimated pI of approximately 9.78. Clone DNA59849-1504 has been deposited with ATCC and is assigned ATCC deposit no. 209986. It is understood that the actual clone has the correct sequence whereas herein are only representations which are prone to minor sequencing errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1155 shows some amino acid sequence identity with the following Dayhoff designations: TKNK_BOVIN; PVB19X587_1; AF019049_1; P_W00948; S72864; P_W00949; I62742; AF038501_1; TKNG_HUMAN; and YAT1_RHOBL. Based on the information provided herein, PRO1155 may play a role in providing neuroprotection and cognitive enhancement.

30 EXAMPLE 113: Isolation of cDNA clones Encoding Human PRO1156

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 138851. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and

assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56261.

In light of an observed sequence homology between the DNA56261 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3675191, the Incyte EST clone 3675191 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 255 and is herein designated as DNA59853-1505.

The full length clone shown in Figure 255' contained a single open reading frame with an apparent translational initiation site at nucleotide positions 212-214 and ending at the stop codon found at nucleotide positions 689-691 (Figure 255; SEQ ID NO:360). The predicted polypeptide precursor (Figure 256, SEQ ID NO:361) is 159 amino acids long. PRO1156 has a calculated molecular weight of approximately 17,476 daltons, an estimated pI of approximately 9.15, a signal peptide sequence at about amino acids 1 to about 22, and potential N-glycosylation sites at about amino acids 27-30 and 41-44.

Clone DNA59853-1505 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209985.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence shown in Figure 256 (SEQ ID NO:361), revealed some homology between the PRO1156 amino acid sequence and the following Dayhoff sequences: D45027_1, P_R79914, JC5309, KBF2_HUMAN, AF010144_1, GEN14351, S68681, P_R79915, ZMTAC 3, and HUMCPGO 1.

20 EXAMPLE 114: Isolation of cDNA Clones Encoding Human PRO1098

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56377.

In light of an observed sequence homology between the DNA56377 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3050917, the Incyte EST clone 3050917 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 257 and is herein designated as DNA59854-1459.

The entire nucleotide sequence of DNA59854-1459 is shown in Figure 257 (SEQ ID NO:362). Clone DNA59854-1459 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 292-294 of SEQ ID NO:362 (Figure 257). The predicted polypeptide precursor is 78 amino acids long (Figure 258). The full-length PRO1098 protein

shown in Figure 258 has an estimated molecular weight of about 8,396 daltons and a pl of about 7.66. Clone DNA59854-1459 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 258, a signal peptide appears to be at about amino acids 1-19 of SEQ ID NO:363, an N-glycosylation site appears to be at about amino acids 37-40 of SEQ ID NO:363, and N-myristoylation sites appear to be at about 15-20, 19-24 and 60-65 of SEQ ID NO:363.

EXAMPLE 115: Isolation of cDNA clones Encoding Human PRO1127

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Scattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57959.

In light of an observed sequence homology between the DNA57959 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 685126, the Merck EST clone 685126 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 259 and is herein designated as DNA60283-1484.

The full length clone shown in Figure 259 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 126-128 and ending at the stop codon found at nucleotide positions 327-329 (Figure 259; SEQ ID NO:364). The predicted polypeptide precursor (Figure 260, SEQ ID NO:365) is 67 amino acids long including a signal peptide at about 1-29 of SEQ ID NO:365. PRO1127 has a calculated molecular weight of approximately 7,528 daltons and an estimated pI of approximately 4.95. Clone DNA60283-1484 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203043. It is understood that the deposited clone has the actual sequence, whereas representations which may have minor sequencing errors are presented herein.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 260 (SEQ ID NO:365), revealed some homology between the PRO1127 amino acid sequence and the following Dayhoff sequences: AF037218_48, P_W09638, HBA_HETPO, S39821, KR2_EBV, CET20D3_8, HCU37630_1, HS193B12_10, S40012 and TRITUBC_1.

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EXAMPLE 116: Isolation of cDNA clones Encoding Human PRO1126

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56250.

In light of an observed sequence homology between the DNA56250 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1437250, the Incyte EST clone 1437250 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 261 and is herein designated as DNA60615-1483.

Clone DNA60615-1483 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 110-112 and ending at the stop codon at nucleotide positions 1316-1318 (Figure 261). The predicted polypeptide precursor is 402 amino acids long (Figure 262). The full-length PRO1126 protein shown in Figure 262 has an estimated molecular weight of about 45,921 daltons and a pI of about 8.60. Analysis of the full-length PRO1126 sequence shown in Figure 262 (SEQ ID NO:367) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25 and potential N-glycosylation sites from about amino acid 66 to about amino acid 69, from about amino acid 138 to about amino acid 141 and from about amino acid 183 to about amino acid 186. Clone DNA60615-1483 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209980.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 262 (SEQ ID NO:367), evidenced significant homology between the PRO1126 amino acid sequence and the following Dayhoff sequences: I73636, NOMR_HUMAN, MMUSMYOC3_1, HS454G6_1, P_R98225, RNU78105_1, RNU72487_1, AF035301_1, CEELC48E7 4 and CEF11C3 3.

EXAMPLE 117: Isolation of cDNA clones Encoding Human PRO1125

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA56540.

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In light of an observed sequence homology between the DNA56540 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1486114, the Incyte EST clone 1486114 was purchased and the cDNA insert was brained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 263 and is herein designated as DNA60615-1483.

The full length clone shown in Figure 263 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 47-49 and ending at the stop codon found at nucleotide positions 1388-1390 (Figure 263; SEQ ID NO:368). The predicted polypeptide precursor (Figure 264, SEQ ID NO:369) is 447 amino acids long. PRO1125 has a calculated molecular weight of approximately 49,798 daltons and an estimated pl of approximately 9.78. Clone DNA60619-1482 has been deposited with ATCC and is assigned 10 ATCC deposit no. 209993. It is understood that the clone has the actual sequence and that the sequences herein are representations based on current techniques which may be prone to minor errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the fulllength sequence, PRO1125 shows some sequence identity with the following Dayhoff designations: RCO1 NEUCR; S58306; PKWA THECU; S76086; P R85881; HET1 PODAN; SPU92792_1; APAF HUMAN; S76414 and S59317.

EXAMPLE 118: Isolation of cDNA clones Encoding Human PRO1186

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56748.

In light of an observed sequence homology between the DNA56748 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3476792, the Incyte EST clone 3476792 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 265 and is herein designated as DNA60621-1516.

The full length clone shown in Figure 265 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 91-93 and ending at the stop codon found at nucleotide positions 406-408 (Figure 265; SEQ ID NO:370). The predicted polypeptide precursor (Figure 266, SEQ ID NO:371) is 105 amino acids long. The signal peptide is at amino acids 1-19 of SEQ ID NO:371. PRO1186 has a calculated molecular weight of approximately 11,715 daltons and an estimated pl of approximately 9.05. Clone DNA60621-1516 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203091.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 266 (SEQ ID NO:371), revealed some sequence identity between the PRO1186 amino acid sequence and the following Dayhoff sequences: VPRA_DENPO, LFE4_CHICK, AF034208_1, AF030433_1, A55035, COL_RABIT, CELB0507_9, S67826_1, S34665 and CRU73817_1.

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EXAMPLE 119: Isolation of cDNA clones Encoding Human PRO1198

An initial DNA sequence referred to herein as DNA52083 was identified using a yeast screen in a human umbilical vein endothelial cell cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA52083 was compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was obtained from human breast skin tissue biopsy. This consensus sequence is designated herein as DNA52780.

In light of an observed sequence homology between the DNA52780 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3852910, the Incyte EST clone 3852910 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 267 and is herein designated as DNA60622-1525.

The full length DNA60622-1525 clone shown in Figure 267 (SEQ ID NO:372) contained a single open reading frame with an apparent translational initiation site at nucleotide positions 54 to 56 and ending at the stop codon found at nucleotide positions 741 to 743. The predicted polypeptide precursor, which is shown in Figure 268 (SEQ ID NO:373), is 229 amino acids long. PRO1198 has a calculated molecular weight of approximately 25,764 daltons and an estimated pl of approximately 9.17. There is a signal peptide sequence at about amino acids 1 through 34. There is sequence identity with glycosyl hydrolases family 31 protein at about amino acids 142 to about 175.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 268 (SEQ ID NO:373), revealed some homology between the PRO1198 amino acid sequence and the following Dayhoff sequences: ATF6H11_6, UCRI_RAT, TOBSUP2NT_1, RCUERF3_1, AMU88186_1, P_W22485, S56579, AF040711_1, DPP4_PIG.

Clone DNA60622-1525 was been deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203090.

EXAMPLE 120: Isolation of cDNA clones Encoding Human PRO1158

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The

homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) r greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57248.

In light of an observed sequence homology between the DNA57248 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2640776, the Incyte EST clone 2640776 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 269 and is herein designated as DNA60625-1507.

The full length clone shown in Figure 269 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 163 to 165 and ending at the stop codon found at nucleotide positions 532 to 534 (Figure 269; SEQ ID NO:374). The predicted polypeptide precursor (Figure 270, SEQ ID NO:375) is 123 amino acids long. PRO1158 has a calculated molecular weight of approximately 13,113 daltons and an estimated pl of approximately 8.53. Additional features include a signal peptide sequence at about amino acids 1-19, a transmembrane domain at about amino acids 56-80, and a potential N-glycosylation site at about amino acids 36-39. Clone DNA60625-1507 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209975.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 270 (SEQ ID NO:375), revealed some homology between the PRO1158 amino acid sequence and the following Dayhoff sequences: ATAC00310510F18A8.10, P_R85151, PHS2_SOLTU, RNMHCIBAC_1, RNA1FMHC_1, I68771, RNRT1A10G_1, PTPA_HUMAN, HUMGACA 1, and CHKPTPA 1.

EXAMPLE 121: Isolation of cDNA clones Encoding Human PRO1159

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single

EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57221.

In light of an observed sequence homology between the DNA57221 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 376776, the Incyte EST clone 376776 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 271 and is herein designated as DNA60627-1508.

Clone DNA60627-1508 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon at nucleotide positions 362-364 (Figure 271). The predicted polypeptide precursor is 90 amino acids long (Figure 272). The full-length PRO1159 protein shown in Figure 272 has an estimated molecular weight of about 9,840 daltons and a pl of about 10.13. Analysis of the full-length PRO1159 sequence shown in Figure 272 (SEQ ID NO:377) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and a potential N-glycosylation site from about amino acid 38 to about amino acid 41. Clone DNA60627-1508 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203092.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 272 (SEQ ID NO:377), evidenced significant homology between the PRO1159 amino acid sequence and the following Dayhoff sequences: AF016494_6, AF036708_20, DSSCUTE_1, D89100_1, S28060, MEFA_XENLA, AF020798_12, G70065, E64423, JQ2005.

EXAMPLE 122: Isolation of cDNA clones Encoding Human PRO1124

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56035.

In light of an observed sequence homology between the DNA56035 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2767646, the Incyte EST clone 2767646 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 273 and is herein designated as DNA60629-1481.

The full length clone shown in Figure 273 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon found at nucleotide positions 2782-2784 (Figure 273; SEQ ID NO:378). The predicted polypeptide precursor (Figure 274, SEQ ID NO:379) is 919 amino acids long. PRO1124 has a calculated molecular weight of approximately 101,282 daltons and an estimated pl of approximately 5.37. Clone DNA60629-1481 has been deposited with the ATCC and is assigned ATCC deposit no. 209979. It is understood that the deposited clone has the actual sequence, whereas only representations based on current sequencing techniques which may include normal and minor errors, are provided herein.

Based on a WU-BLAST2 sequence alignment analysis of the full-length sequence, PRO1124 shows significant amino acid sequence identity to a chloride channel protein and to ECAM-1. Specifically, the following Dayhoff designations were identified as having sequence identity with PRO1124: ECLC_BOVIN,

AF001261_1, P_W06548, SSC6A10_1, AF004355_1, S76691, AF017642, BYU06866_2, CSA_DICDI and SAU47139_2.

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1287

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the fringe protein. This EST sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence obtained is herein designated DNA40568.

Based on the DNA40568 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1287. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, supra, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCGGGGAAAGGGACTTGATGTTGG-3' (SEQ ID NO:382)

reverse PCR primer 1 5'-GCGAAGGTGAGCCTCTATCTCGTGCC-3' (SEQ ID NO:383)

25 reverse PCR primer 2 5'-CAGCCTACACGTATTGAGG-3' (SEQ ID NO:384)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40568 sequence which had the following nucleotide sequence

hybridization probe

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5'-CAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCC-3' (SEQ ID NO:385).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1287 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a Notl site, linked with blunt to Sall hemikinased adaptors, cleaved with Notl, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD;

pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., <u>Science</u>, <u>253</u>:1278-1280 (1991)) in the unique Xhol and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1287 (designated herein as DNA61755-1554 [Figure 275, SEQ ID NO:380]) and the derived protein sequence for PRO1287.

The entire nucleotide sequence of DNA61755-1554 is shown in Figure 275 (SEQ ID NO:380). The full length clone contained a single open reading frame with an apparent translational initiation site at nucleotide positions 655-657 and a stop signal at nucleotide positions 2251-2253 (Figure 275, SEQ ID NO:380). The predicted polypeptide precursor is 532 amino acids long, has a calculated molecular weight of approximately 61,351 daltons and an estimated pI of approximately 8.77. Analysis of the full-length PRO1287 sequence shown in Figure 276 (SEQ ID NO:381) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27 and potential N-glycosylation sites from about amino acid 315 to about amino acid 318 and from about amino acid 324 to about amino acid 327. Clone DNA61755-1554 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203112.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 276 (SEQ ID NO:381), evidenced significant homology between the PRO1287 amino acid sequence and the following Dayhoff sequences: CET24D1_1, EZRI_BOVIN, GGU19889_1, CC3_YEAST, S74244, NALS_MOUSE, MOES_PIG, S28660, S44860 and YNA4_CAEEL.

20 EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1312

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DNA55773 was identified in a human fetal kidney cDNA library using a yeast screen that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA55773 sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1312.

The full length DNA61873-1574 clone shown in Figure 277 (SEQ ID NO:386) contained a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 and ending at the stop codon found at nucleotide positions 643-645. The predicted polypeptide precursor is 212 amino acids long (Figure 278, SEQ ID NO:387). PRO1312 has a calculated molecular weight of approximately 24,024 daltons and an estimated pl of approximately 6.26. Other features include a signal peptide at about amino acids 1-14; a transmembrane domain at about amino acids 141-160, and potential N-glycosylation sites at about amino acids 76-79 and 93-96.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 278 (SEQ ID NO:387), revealed some homology between the PRO1312 amino acid sequence and the following Dayhoff sequences: GCINTALPH_1, GIBMUC1A_1, P_R96298, AF001406_1, PVU88874_1, P_R85151, AF041409_1, CELC50F2_7, C45875, and AB009510_21.

Clone DNA61873-1574 has been deposited with ATCC and is assigned ATCC deposit no. 203132.

EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1192

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA35924. Based on the DNA35924 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1192.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CCGAGGCCATCTAGAGGCCAGAGC-3' (SEQ ID NO:390)

reverse PCR primer: 5'-ACAGGCAGAGCCAATGGCCAGAGC-3' (SEQ ID NO:391).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35924 sequence which had the following nucleotide sequence:

hybridization probe:

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5'-GAGAGGACTGCGGGAGTTTGGGACCTTTGTGCAGACGTGCTCATG-3' (SEQ ID NO:392).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1192 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver and spleen tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1192 designated herein as DNA62814-1521 and shown in Figure 279 (SEQ ID NO:388); and the derived protein sequence for PRO1192 which is shown in Figure 280 (SEQ ID NO:389).

The entire coding sequence of PRO1192 is shown in Figure 279 (SEQ ID NO:388). Clone DNA62814-1521 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 766-768. The predicted polypeptide precursor is 215 amino acids long. The predicted polypeptide precursor has the following features: a signal peptide at about amino acids 1-21; a transmembrane domain at about amino acids 153-176; potential N-glycosylation sites at about amino acids 39-42 and 118-121; and homology with myelin P0 proteins at about amino acids 27-68 and 99-128 of Figure 280. The full-length PRO1192 protein shown in Figure 280 has an estimated molecular weight of about 24,484 daltons and a pI of about 6.98.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 280 (SEQ ID NO:389), revealed homology between the PRO1192 amino acid sequence and the following Dayhoff sequences: GEN12838, MYP0_HUMAN, AF049498_1, GEN14531, P_W14146, HS46KDA_1, CINB_RAT, OX2G_RAT, D87018_1, and D86996_2.

Clone DNA62814-1521 was deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203093.

EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1160

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above This consensus sequence is herein designated DNA40650. Based on the DNA40650 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1160.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCTCCCTGATCTTCATGTCACCACC-3' (SEQ ID NO:395)

reverse PCR primer 5'-CAGGGACACACTCTACCATTCGGGAG-3' (SEQ ID NO:396)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40650 sequence which had the following nucleotide sequence

hybridization probe

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5'-CCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTC-3' (SEQ ID NO:397)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1160 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1160 (designated herein as DNA62872-1509 [Figure 281, SEQ ID NO: 393]) and the derived protein sequence for PRO1160.

The entire nucleotide sequence of DNA62872-1509 is shown in Figure 281 (SEQ ID NO:393). Clone DNA62872-1509 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 310-312 (Figure 281). The predicted polypeptide precursor is 90 amino acids long (Figure 282). The full-length PRO1160 protein shown in Figure 282 has an estimated molecular weight of about 9,039 daltons and a pl of about 4.37. Analysis of the full-length PRO1160 sequence shown in Figure 282 (SEQ ID NO:394) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and a protein kinase C phosphorylation site from about amino acid 68 to about amino acid 70. Clone DNA62872-1509 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203100.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 282 (SEQ ID NO:394), evidenced significant homology between the PRO1160 amino acid sequence and the following Dayhoff sequences: B30305, GEN13490, I53641, S53363, HA34_BRELC, SP96_DICDI, S36326, SSU51197_10, MUC1_XENLA, TCU32448_1 and AF000409_1.

35 EXAMPLE 127: Isolation of cDNA clones Encoding Human PRO1187

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of

expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57726.

In light of an observed sequence homology between the DNA57726 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 358563, the Incyte EST clone 358563 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 283 and is herein designated as DNA62876-1517.

The full length clone shown in Figure 283 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon found at nucleotide positions 481-483 (Figure 283; SEQ ID NO:398). The predicted polypeptide precursor (Figure 284, SEQ ID NO:399) is 120 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:399. PRO1187 has a calculated molecular weight of approximately 12,925 daltons and an estimated pl of approximately 9.46. Clone DNA62876-1517 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203095. It is understood that the deposited clone contains the actual sequence and that the representations herein may have minor sequencing errors.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 284 (SEQ ID NO:399), revealed some sequence identity (and therefore some relation) between the PRO1187 amino acid sequence and the following Dayhoff sequences: MGNENDOBX_1, CELF41G3_9, AMPG_STRL1, HSBBOVHERL_2, LEEXTEN10_1, AF029958_1 and P_W04957.

25 EXAMPLE 128: Isolation of cDNA clones Encoding Human PRO1185

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56426.

In light of an observed sequence homology between the DNA56426 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3284411, the Incyte EST clone 3284411 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 285 and is herein designated as DNA62881-1515.

The full length DNA62881-1515 clone shown in Figure 285 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 4-6 and ending at the stop codon found at nucleotide positions 598-600 (Figure 285; SEQ ID NO:400). The predicted polypeptide precursor (Figure 286, SEQ ID NO:401) is 198 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:401. PRO1185 has a calculated molecular weight of approximately 22,105 daltons and an estimated pl of approximately 7.73. Clone DNA62881-1515 has been deposited with the ATCC and is assigned ATCC deposit no. 203096.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 286 (SEQ ID NO:401), revealed some sequence identity between the PRO1185 amino acid sequence and the following Dayhoff sequences: TUP1_YEAST, AF041382_1, MAOM_SOLTU, SPPBPHU9_1,I41024, EPCPLCFAIL_1, HSPLEC_1, YKL4_CAEEL, A44643, TGU65922 1.

EXAMPLE 129: Isolation of cDNA clones Encoding Human PRO1345

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA47364. Based on the DNA47364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1345.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTGGTTATCCCCAGGAACTCCGAC-3' (SEQ ID NO:404)

reverse PCR primer 5'-CTCTTGCTGCTGCGACAGGCCTC-3' (SEQ ID NO:405)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47364 sequence which had the following nucleotide sequence

25 <u>hybridization probe</u>

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5'-CGCCCTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGAC-3' (SEQ ID NO:406)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1345 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1345 (designated herein as DNA64852-1589 [Figure 287, SEQ ID NO:402]) and the derived protein sequence for PRO1345.

The entire nucleotide sequence of DNA64852-1589 is shown in Figure 287 (SEQ ID NO:402). Clone DNA64852-1589 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 or 34-36 and ending at the stop codon at nucleotide positions 625-627 (Figure 287). The predicted polypeptide precursor is 206 amino acids long (Figure 288). The full-length PRO1345 protein shown in Figure

288 has an estimated molecular weight of about 23,190 daltons and a pl of about 9.40. Analysis of the full-length PRO1345 sequence shown in Figure 288 (SEQ ID NO:403) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 or from about amino acid 10 to about amino acid 31 and a C-type lectin domain signature sequence from about amino acid 176 to about amino acid 190. Clone DNA64852-1589 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203127.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 288 (SEQ ID NO:403), evidenced significant homology between the PRO1345 amino acid sequence and the following Dayhoff sequences: BTU22298_1, TETN_CARSP, TETN_HUMAN, MABA_RAT, S34198, P_W13144, MACMBPA_1, A46274, PSPD_RAT AND P_R32188.

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EXAMPLE 130: Isolation of cDNA clones Encoding Human PRO1245

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56019.

In light of an observed sequence homology between the DNA56019 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1327836, the Incyte EST clone 1327836 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 289 and is herein designated as DNA64884-1527.

The full length clone shown in Figure 289 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 391-393 (Figure 289; SEQ ID NO:407). The predicted polypeptide precursor (Figure 290, SEQ ID NO:408) is 104 amino acids long, with a signal peptide sequence at about amino acid 1 to about amino acid 18. PRO1245 has a calculated molecular weight of approximately 10,100 daltons and an estimated pl of approximately 8.76.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 290 (SEQ ID NO:408), revealed some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA_THETH, GEN11167, MTV044_4, AB011151_1, RLAJ2750_3, SNELIPTRA_1, S63624, C28391, A37907, and S14064.

Clone DNA64884-1245 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

EXAMPLE 131: Isolation of cDNA clones Encoding Human PRO1358

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 88718, the Incyte EST clone 88718 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 291 and is herein designated as DNA64890-1612.

The full length clone shown in Figure 291 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86 through 88 and ending at the stop codon found at nucleotide positions 1418 through 1420 (Figure 291; SEQ ID NO:409). The predicted polypeptide precursor (Figure 292, SEQ ID NO:410) is 444 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:410. PRO1358 has a calculated molecular weight of approximately 50,719 daltons and an estimated pl of approximately 8.82. Clone DNA64890-1612 was deposited with the ATCC on August 18, 1998 and is assigned ATCC deposit no. 203131.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 292 (SEQ ID NO:410), revealed sequence identity between the PRO1358 amino acid sequence and the following Dayhoff sequences: P_W07607, AB000545_1, AB000546_1, A1AT_RAT, AB015164_1, P_P50021, COTR_CAVPO, and HAMHPP_1. The variants claimed in this application exclude these sequences.

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EXAMPLE 132: Isolation of cDNA clones Encoding Human PRO1195

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55716.

In light of an observed sequence homology between the DNA55716 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3252980, the Incyte EST clone 3252980 was purchased

and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 293 and is herein designated as DNA65412-1523.

The full length clone shown in Figure 293 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon found at nucleotide positions 511-513 (Figure 293; SEQ ID NO:411). The predicted polypeptide precursor (Figure 294, SEQ ID NO:412) is 151 amino acids long. The signal sequence is at about amino acids 1-22 of SEQ ID NO:412. PRO1195 has a calculated molecular weight of approximately 17,277 daltons and an estimated pI of approximately 5.33. Clone DNA65412-1523 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203094.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 294 (SEQ ID NO:412), revealed some sequence identity between the PRO1195 amino acid sequence and the following Dayhoff sequences: MMU28486_1, AF044205_1, P_W31186, CELK03C7_1, F69034, EF1A_METVA, AF024540_1, SSU90353_1, MRSP_STAAU and P_R97680.

EXAMPLE 133: Isolation of cDNA clones Encoding Human PRO1270

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57951.

In light of an observed sequence homology between the DNA57951 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 124878, the Merck EST clone 124878 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 295 and is herein designated as DNA66308-1537.

Clone DNA66308-1537 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 103-105 and ending at the stop codon at nucleotide positions 1042-1044 (Figure 295). The predicted polypeptide precursor is 313 amino acids long (Figure 296). The full-length PRO1270 protein shown in Figure 296 has an estimated molecular weight of about 34,978 daltons and a pI of about 5.71. Analysis of the full-length PRO1270 sequence shown in Figure 296 (SEQ ID NO:414) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a potential N-glycosylation site from about amino acid 163 to about amino acid 166 and glycosaminoglycan attachment sites from about amino acid 74 to about amino acid 77 and from about amino acid 289 to about amino acid 292. Clone DNA66308-1537 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203159.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 296 (SEQ ID NO:414), evidenced significant homology between the PRO1270 amino acid sequence and the following Dayhoff sequences: XLU86699_1, S49589, FIBA_PARPA, FIBB_HUMAN, P_R47189, AF004326_1, DRTENASCN_1, AF004327_1, P_W01411 and FIBG_BOVIN.

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EXAMPLE 134: Isolation of cDNA clones Encoding Human PRO1271

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57955.

In light of an observed sequence homology between the DNA57955 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA625350, the Merck EST clone AA625350 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 297 and is herein designated as DNA66309-1538.

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Clone DNA66309-1538 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 718-720 (Figure 297). The predicted polypeptide precursor is 208 amino acids long (Figure 298). The full-length PRO1271 protein shown in Figure 298 has an estimated molecular weight of about 21,531 daltons and a pI of about 8.99. Analysis of the full-length PRO1271 sequence shown in Figure 298 (SEQ ID NO:416) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 and a transmembrane domain from about amino acid 166 to about amino acid 187. Clone DNA66309-1538 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203235.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 298 (SEQ ID NO:416), evidenced significant homology between the PRO1271 amino acid sequence and the following Dayhoff sequences: S57180, S63257, AGA1_YEAST, BPU43599_1, YS8A_CAEEL, S67570, LSU54556_2, S70305, VGLX_HSVEB, and D88733_1.

EXAMPLE 135: Isolation of cDNA clones Encoding Human PRO1375

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A Merck/Wash. U. database was searched and a Merck EST was identified. This sequence was then put in a program which aligns it with other seequences from the Swiss-Prot public database, public EST databases (e.g., GenBank, Merck/Wash. U.), and a proprietary EST database (LIFESEQ®, Incyte

Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA67003".

Based on the DNA 67003 consensus sequence, the nucleic acid (SEQ ID NO:417) was identified in a human pancreas library. DNA sequencing of the clone gave the full-length DNA sequence for PRO1375 and the derived protein sequence for PRO1375.

The entire coding sequence of PRO1375 is shown in Figure 299 (SEQ ID NO:417). Clone DNA67004-1614 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 104-106 and an apparent stop codon at nucleotide positions 698-700 of SEQ ID NO:417. The predicted polypeptide precursor is 198 amino acids long. The transmembrane domains are at about amino acids 11-28 (type II) and 103-125 of SEQ ID NO:418. Clone DNA67004-1614 has been deposited with ATCC and is assigned ATCC deposit no. 203115. The full-length PRO1375 protein shown in Figure 300 has an estimated molecular weight of about 22,531 daltons and a pI of about 8.47.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 300 (SEQ ID NO:418), revealed sequence identity between the PRO1375 amino acid sequence and the following Dayhoff sequences: AF026198_5, CELR12C12_5, S73465, Y011_MYCPN, S64538_1, P_P8150, MUVSHPO10_1, VSH_MUMPL and CVU59751_5.

EXAMPLE 136: Isolation of cDNA clones Encoding Human PRO1385

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57952.

In light of an observed sequence homology between the DNA57952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3129630, the Incyte EST clone 3129630 was purchased and the cDNA insert was brained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 301 and is herein designated as DNA68869-1610.

Clone DNA68869-1610 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 410-412 (Figure 301). The predicted polypeptide precursor is 128 amino acids long (Figure 302). The full-length PRO1385 protein shown in Figure 302 has an estimated molecular weight of about 13,663 daltons and a pl of about 10.97. Analysis of the full-length PRO1385 sequence shown in Figure 302 (SEQ ID NO:420) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, and glycosylaminoglycan attachment sites from about amino acid 82 to about amino acid 85 and from about amino acid 91 to about amino acid 94. Clone DNA68869-1610 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203164.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 302 (SEQ ID NO:420), evidenced low homology between the PRO1385 amino acid sequence and the following Dayhoff sequences: CELT14A8_1, LMNACHRA1_1, HXD9_HUMAN, CHKCMLF_1, HS5PP34_2, DMDRING_1, A37107_1, MMLUNGENE_1, PUM_DROME and DMU25117_1.

15 EXAMPLE 137: Isolation of cDNA clones Encoding Human PRO1387

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56259.

In light of an observed sequence homology between the DNA56259 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3507924, the Incyte EST clone 3507924 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 303 and is herein designated as DNA68872-1620.

Clone DNA68872-1620 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 85-87 and ending at the stop codon at nucleotide positions 1267-1269 (Figure 303). The predicted polypeptide precursor is 394 amino acids long (Figure 304). The full-length PRO1387 protein shown in Figure 304 has an estimated molecular weight of about 44,339 daltons and a pI of about 7.10. Analysis of the full-length PRO1387 sequence shown in Figure 304 (SEQ ID NO:422) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 275 to about amino acid 296, potential N-glycosylation sites from about amino acid 76 to about amino acid 79, from about amino acid 231 to about amino acid 234, from about amino acid 302 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid

379, and amino acid sequence blocks having homology to myelin p0 protein from about amino acid 210 to about amino acid 239 and from about amino acid 92 to about amino acid 121. Clone DNA68872-1620 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203160.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 304 (SEQ ID NO:422), evidenced significant homology between the PRO1387 amino acid sequence and the following Dayhoff sequences: P_W36955, MYPO_HETFR, HS46KDA_1, AF049498_1, MYOO_HUMAN, AF030454_1, A53268, SHPTCRA_1, P W14146 and GEN12838.

EXAMPLE 138: Isolation of cDNA clones Encoding Human PRO1384

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA54192. Based on the DNA54192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1384.

PCR primers (forward and reverse) were synthesized:

5 <u>forward PCR primer</u> 5'-TGCAGCCCCTGTGACACAAACTGG-3' (SEQ ID NO:425)

reverse PCR primer 5'-CTGAGATAACCGAGCCATCCTCCCAC-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA54192 sequence which had the following nucleotide sequence:

hybridization probe

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20 5'-GGAGATAGCTGCTATGGGTTCTTCAGGCACAACTTAACATGGGAAG-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1384 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1384 (designated herein as DNA71159-1617 [Figure 305, SEQ ID NO:423]; and the derived protein sequence for PRO1384.

The entire coding sequence of PRO1384 is shown in Figure 305 (SEQ ID NO:423). Clone DNA71159-1617 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 182-184 and an apparent stop codon at nucleotide positions 869-871. The predicted polypeptide precursor is 229 amino acids long. The full-length PRO1384 protein shown in Figure 306 has an estimated molecular weight of about 26,650 daltons and a pI of about 8.76. Additional features include a type II transmembrane domain at about amino acids 32-57, and potential N-glycosylation sites at about amino acids 68-71, 120-123, and 134-137.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

35 alignment analysis of the full-length sequence shown in Figure 306 (SEQ ID NO:424), revealed homology
between the PRO1384 amino acid sequence and the following Dayhoff sequences: AF054819_1, HSAJ1687_1,
AF009511_1,AB010710_1,GEN13595, HSAJ673_1,GEN13961,AB005900_1,LECH_CHICK,AF021349_1,

and NK13_RAT.

Clone DNA71159-1617 has been deposited with ATCC and is assigned ATCC deposit no. 203135.

EXAMPLE 139: Use of PRO as a hybridization probe

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

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EXAMPLE 140: Expression of PRO in E. coli

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in E. coli.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for amplicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., <u>supra</u>. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the

protein.

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PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate•2H2O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin

from the samples.

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Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 141: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μ g pRK5-PRO DNA is mixed with about 1 μ g DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 μ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl₂. To this mixture is added, dropwise, 500 μ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO₄, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 μ Ci/ml ³⁵S-cysteine and 200 μ Ci/ml ³⁵S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Somparyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 μ g/ml bovine insulin and 0.1 μ g/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO₄ or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ³⁵S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a polyhis tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni²⁺-chelate affinity chromatography.

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PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., <u>Current Protocols of Molecular Biology</u>, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., <u>Nucl. Acids Res.</u> 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect[®] (Quiagen), Dosper[®] or Fugene[®] (Boehringer Mannheim). The cells are grown as described in Lucas et al., <u>supra</u>. Approximately 3 x 10⁻⁷ cells are frozen in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μ m filtered PS20 with 5% 0.2 μ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3 x 10⁵ cells/mL. The cell media is exchanged with fresh media by

centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2×10^6 cells/mL. On day 0, the cell number pH ie determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

25 EXAMPLE 142: Expression of PRO in Yeast

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The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

5 EXAMPLE 143: Expression of PRO in Baculovirus-Infected Insect Cells

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The following method describes recombinant expression of PRO in Baculovirus-infected insect cells. The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., <u>Baculovirus expression vectors: A Laboratory Manual</u>, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni²⁺-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl₂; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni²⁺-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A₂₈₀ with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A₂₈₀ baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni²⁺-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His₁₀-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 144: Preparation of Antibodies that Bind PRO

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This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, <u>supra</u>. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

EXAMPLE 145: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSETM (Pharmacia LKB Biotechnology). The antibody

is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (e.g., a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

EXAMPLE 146: Drug Screening

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This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (I) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the

solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

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EXAMPLE 147: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (i.e., a PRO polypeptide) or of small molecules with which they interact, e.g., agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide in vivo (c.f., Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, <u>Biochemistry</u>, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, <u>J. Biochem.</u>, <u>113</u>:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

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Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 2

5	<u>Material</u>	ATCC Dep. No.	Deposit Date
	DNA16422-1209	209929	June 2, 1998
	DNA16435-1208	209930	June 2, 1998
	DNA21624-1391	209917	June 2, 1998
	DNA23334-1392	209918	June 2, 1998
10	DNA26288-1239	209792	April 21, 1998
	DNA26843-1389	203099	August 4, 1998
	DNA26844-1394	209926	June 2, 1998
	DNA30862-1396	209920	June 2, 1998
	DNA35680-1212	209790	April 21, 1998
15	DNA40621-1440	209922	June 2, 1998
	DNA44161-1434	209907	May 27, 1998
	DNA44694-1500	203114	August 11, 1998
	DNA45495-1550	203156	August 25, 1998
	DNA47361-1154	209431	November 7, 1997
20	DNA47394-1572	203109	August 11, 1998
	DNA48320-1433	209904	May 27, 1998
	DNA48334-1435	209924	June 2, 1998
	DNA48606-1479	203040	July 1, 1998
	DNA49141-1431	203003	June 23, 1998
25	DNA49142-1430	203002	June 23, 1998
	DNA49143-1429	203013	June 23, 1998
	DNA49647-1398	209919	June 2, 1998
	DNA49819-1439	209931	June 2, 1998
•	DNA49820-1427	209932	June 2, 1998
30	DNA49821-1562	209981	June 16, 1998
	DNA52192-1369	203042	July 1, 1998
	DNA52598-1518	203107	August 11, 1998
	DNA53913-1490	203162	August 25, 1998
25	DNA53978-1443	209983	June 16, 1998
35	DNA53996-1442	209921	June 2, 1998
	DNA56041-1416	203012	June 23, 1998
	DNA56047-1456	209948	June 9, 1998
	DNA56050-1455	203011	June 23, 1998
40	DNA56112-1437	203113	August 11, 1998
40	DNA56113-1378	203049	July 1, 1998
	DNA56410-1414	209923	June 2, 1998
	DNA56436-1448 DNA56855-1447	209902	May 27, 1998
	DNA56859-1445	203004	June 23, 1998
45	DNA56860-1510	203019	June 23, 1998
43		209952	June 9, 1998
	DNA56865-1491	203022	June 23, 1998
	DNA56866-1342 DNA56868-1209	203023	June 23, 1998
		203024	June 23, 1998
50	DNA56869-1545	203161	August 25, 1998
20	DNA56870-1492 DNA57033-1403	209925	June 2, 1998
	DNA57033-1403 DNA57037-1444	209905	May 27, 1998
	DNA57129-1413	209903	May 27, 1998
	DIAD/1127-1413	209977	June 16, 1998

		200050	I 0 1000
	DNA57690-1374	209950	June 9, 1998
	DNA57693-1424	203008	June 23, 1998
	DNA57694-1341	203017	June 23, 1998
	DNA57695-1340	203006	June 23, 1998
	DNA57699-1412	203020	June 23, 1998
5	DNA57702-1476	209951	June 9, 1998
	DNA57704-1452	209953	June 9, 1998
	DNA57708-1411	203021	June 23, 1998
	DNA57710-1451	203048	July 1, 1998
	DNA57711-1501	203047	July 1, 1998
10	DNA57827-1493	203045	July 1, 1998
	DNA57834-1339	209954	June 9, 1998
	DNA57836-1338	203025	June 23, 1998
	DNA57838-1337	203014	June 23, 1998
	DNA57844-1410	203010	June 23, 1998
15	DNA58721-1475	203110	August 11, 1998
	DNA58723-1588	203133	August 18, 1998
	DNA58737-1473	203136	August 18, 1998
	DNA58743-1609	203154	August 25, 1998
	DNA58846-1409	209957	June 9, 1998
20	DNA58848-1472	209955	June 9, 1998
20	DNA58849-1494	209958	June 9, 1998
	DNA58850-1495	209956	June 9, 1998
	DNA58853-1423	203016	June 23, 1998
	DNA58855-1422	203018	June 23, 1998
25	DNA59205-1421	203009	June 23, 1998
23	DNA59211-1450	209960	June 9, 1998
	DNA59213-1487	209959	June 9, 1998
	DNA59214-1449	203046	July 1, 1998
	DNA59215-1425	209961	June 9, 1998
30	DNA59220-1514	209962	June 9, 1998
50	DNA59488-1603	203157	August 25, 1998
•	DNA59493-1420	203050	July 1, 1998
	DNA59497-1496	209941	June 4, 1998
	DNA59588-1571	203106	August 11, 1998
35	DNA59603-1419	209944	June 9, 1998
33	DNA59605-1418	203005	June 23, 1998
	DNA59606-1471	209945	June 9, 1998
	DNA59607-1497	209957	June 9, 1998
	DNA59609-1470	209963	June 9, 1998
40		209990	June 16, 1998
40	DNA59610-1559	209947-	June 9, 1998
	DNA59612-1466	203007	June 23, 1998
	DNA59613-1417	209991	June 16, 1998
	DNA59616-1465		July 1, 1998
15	DNA59619-1464	¹ 203041 209989	June 16, 1998
45	DNA59620-1463	209999	June 17, 1998
	DNA59625-1498		
	DNA59767-1489	203108	August 11, 1998
	DNA59776-1600	203128	August 18, 1998
	DNA59777-1480	203111	August 11, 1998
50	DNA59820-1549	203129	August 18, 1998
	DNA59827-1426	203089	August 4, 1998
	DNA59828-1608	203158	August 25, 1998
	DNA59838-1462	209976	June 16, 1998
	DNA59839-1461	209988	June 16, 1998
55	DNA59841-1460	203044	July 1, 1998
	DNA59842-1502	209982	June 16, 1998

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	DNA59846-1503	209978	June 16, 1998
	DNA59847-1511	203098	August 4, 1998
	DNA59848-1512	203088	August 4, 1998
	DNA59849-1504	209986	June 16, 1998
	DNA59853-1505	209985	June 16, 1998
5	DNA59854-1459	209974	June 16, 1998
	DNA60283-1484	203043	July 1, 1998
	DNA60615-1483	209980	June 16, 1998
	DNA60619-1482	209993	June 16, 1998
	DNA60621-1516	203091	August 4, 1998
10	DNA60622-1525	203090	August 4, 1998
	DNA60625-1507	209975	June 16, 1998
	DNA60627-1508	203092	August 4, 1998
	DNA60629-1481	209979	June 16, 1998
	DNA61755-1554	203112	August 11, 1998
15	DNA61873-1574	203132	August 18, 1998
	DNA62814-1521	203093	August 4, 1998
	DNA62872-1509	203100	August 4, 1998
	DNA62876-1517	203095	August 4, 1998
	DNA62881-1515	203096	August 4, 1998
20	DNA64852-1589	203127	August 18, 1998
	DNA64884-1527	203155	August 25, 1998
	DNA64890-1612	203131	August 18, 1998
	DNA65412-1523	203094	August 4, 1998
	DNA66308-1537	203159	August 25, 1998
25	DNA66309-1538	203235	September 15, 1998
	DNA67004-1614	203115	August 11, 1998
	DNA68869-1610	203164	August 25, 1998
	DNA68872-1620	203160	August 25, 1998
	DNA71159-1617	203135	August 18, 1998
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These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

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The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the

deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

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1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting f the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEO ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEO ID NO:84), Figure 49 (SEO ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEO ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEO ID NO:119), 10 Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEO ID NO:160). Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEO ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEO ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEO ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEO ID NO:231). Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEO ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEO ID NO:256). Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID-NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ

ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422) and Figure 306 (SEO ID NO:424).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide 5 sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEO ID NO:32), Figure 24 (SEO ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), 10 Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEO ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEO ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 15 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEO ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ 20 ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ 25 ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEO ID NO:294), Figure 213 (SEO ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEO ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEO 35 ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372),

Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

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3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEO ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEO ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEO ID NO:145). Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID

NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) or Figure 305 (SEQ ID NO:423).

- Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 2.
 - 5. A vector comprising the nucleic acid of Claim 1.
- 15 6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.
 - 7. A host cell comprising the vector of Claim 5.
- 20 8. The host cell of Claim 7 wherein said cell is a CHO cell.
 - 9. The host cell of Claim 7 wherein said cell is an E. coli.
 - 10. The host cell of Claim 7 wherein said cell is a yeast cell.

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- 11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.
- 12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68

(SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEO ID NO:135), Figure 79 (SEO ID NO:138), Figure 83 (SEO ID NO:146), Figure 85 (SEO ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEO ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ 10 ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEO ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEO ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEO ID NO:262), Figure 182 (SEO ID NO:264), Figure 184 (SEO ID NO:266), Figure 186 (SEO 15 ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), 20 Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ 25 ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), 30 Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422) and Figure 306 (SEQ ID NO:424).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 2.

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14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.

- 16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.
 - 17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.
 - 18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.
- 10 19. The antibody of Claim 17 wherein said antibody is a humanized antibody.

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- 20. The antibody of Claim 17 wherein said antibody is an antibody fragment.
- An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid 21. 15 which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEO ID NO:29), Figure 22 (SEO ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEO ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure

191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEO ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEO ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEO ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEO ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEO ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

22. An isolated nucleic acid molecule which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID 20 NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEO ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEO ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEO ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 35 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID

NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEO ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEO ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

- 20 23. An isolated extracellular domain of of PRO polypeptide.
 - 24. An isolated PRO polypeptide lacking its associated signal peptide.
- 25. An isolated polypeptide having at least about 80% amino acid sequence identity to an extracellular domain of of PRO polypeptide.
 - 26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO polypeptide lacking its associated signal peptide.

FIGURE 1

CGGACGCGTGCGTGCGAGGCGAAGGTGACCGGGGACCGAGCATTTCAGATCTGCTCGGTAGA CCTGGTGCACCACCACCATGTTGGCTGCAAGGCTGGTGTCTCCCGGACACTACCTTCTAGG GTTTTCCACCCAGCTTTCACCAAGGCCTCCCCTGTTGTGAAGAATTCCATCACGAAGAATCA ATGGCTGTTAACACCTAGCAGGGAATATGCCACCAAAACAAGAATTGGGATCCGGCGTGGGA GAACTGGCCAAGAACTCAAAGAGGCAGCATTGGAACCATCGATGGAAAAAATATTTAAAATT GATCAGATGGGAAGATGGTTTGTTGCTGGAGGGGCTGCTGTTGGTCTTTGGAGCATTGTGCTA CTATGGCTTGGGACTGTCTAATGAGATTGGAGCTATTGAAAAGGCTGTAATTTGGCCTCAGT ATGTCAAGGATAGAATTCATTCCACCTATATGTACTTAGCAGGGAGTATTGGTTTAACAGCT TTGTCTGCCATAGCAATCAGCAGAACGCCTGTTCTCATGAACTTCATGATGAGAGGCTCTTG GGTGACAATTGGTGTGACCTTTGCAGCCATGGTTGGAGCTGGAATGCTGGTACGATCAATAC CATATGACCAGAGCCCAGAGCATCTTGCTTGCTTGCTACATTCTGGTGTGATGGGT GCAGTGGTGGCTCCTCTGACAATATTAGGGGGTCCTCTTCTCATCAGAGCTGCATGGTACAC AGCTGGCATTGTGGGAGGCCTCTCCACTGTGGCCATGTGTGCGCCCAGTGAAAAGTTTCTGA ACATGGGTGCACCCCTGGGAGTGGGCCTGGGTCTCGTCTTTGTGTCCTCATTGGGATCTATG TTTCTTCCACCTACCACCGTGGCTGGTGCCACTCTTTACTCAGTGGCAATGTACGGTGGATT AGTTCTTTCAGCATGTTCCTTCTGTATGATACCCAGAAAGTAATCAAGCGTGCAGAAGTAT CACCAATGTATGGAGTTCAAAAATATGATCCCATTAACTCGATGCTGAGTATCTACATGGAT AAGTGACTCAGCTTCTGGCTTCTCTGCTACATCAAATATCTTGTTTAATGGGGCAGATATGC ATTAAATAGTTTGTACAAGCAGCTTTCGTTGAAGTTTAGAAGATAAGAAACATGTCATCATA TTTAAATGTTCCGGTAATGTGATGCCTCAGGTCTGCCTTTTTTTCTGGAGAATAAATGCAGT AATCCTCTCCCAAATAAGCACACACATTTTCAATTCTCATGTTTGAGTGATTTTAAAATGTT TTGGTGAATGTGAAAACTAAAGTTTGTGTCATGAGAATGTAAGTCTTTTTTCTACTTTAAAA TTTAGTAGGTTCACTGAGTAACTAAAATTTAGCAAACCTGTGTTTTGCATATTTTTTTGGAGT GCAGAATATTGTAATTAATGTCATAAGTGATTTGGAGCTTTGGTAAAGGGACCAGAGAGAAG GAGTCACCTGCAGTCTTTTGTTTTTTTAAATACTTAGAACTTAGCACTTGTGTTATTGATTA GCTGAACTTAACAAAACTGTTCATCCTGAAACAGGCACAGGTGATGCATTCTCCTGCTGTTG CTTCTCAGTGCTCTTTCCAATATAGATGTGGTCATGTTTGACTTGTACAGAATGTTAATC ATACAGAGAATCCTTGATGGAATTATATATGTGTGTTTTTACTTTTGAATGTTACAAAAGGAA ATAACTTTAAAACTATTCTCAAGAGAAAATATTCAAAGCATGAAATATGTTGCTTTTTCCAG **AATACAAACAGTATACTCATG**

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FIGURE 2

MLAARLVCLRTLPSRVFHPAFTKASPVVKNSITKNQWLLTPSREYATKTRIGIRRGRTGQEL
KEAALEPSMEKIFKIDQMGRWFVAGGAAVGLGALCYYGLGLSNEIGAIEKAVIWPQYVKDRI
HSTYMYLAGSIGLTALSAIAISRTPVLMNFMMRGSWVTIGVTFAAMVGAGMLVRSIPYDQSP
GPKHLAWLLHSGVMGAVVAPLTILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPL
GVGLGLVFVSSLGSMFLPPTTVAGATLYSVAMYGGLVLFSMFLLYDTQKVIKRAEVSPMYGV
QKYDPINSMLSIYMDTLNIFMRVATMLATGGNRKK

FIGURE 3

GAAGGCTGCCTCGCTGGTCCGAATTCGGTGGCGCCACGTCCGCCCGTCTCCGCCTTCTGCAT GGTCGGCACGGGGAGTCGGGCGGTCTTGTGCATCTTGGCTACCTGTGGGTCGAAG<u>ATG</u>TCGG ACATCGGAGACTGGTTCAGGAGCATCCCGGCGATCACGCGCTATTGGTTCGCCGCCACCGTC GCCGTGCCCTTGGTCGGCAAACTCGGCCTCATCAGCCCGGCCTACCTCTTCCTCTGGCCCGA AGCCTTCCTTTATCGCTTTCAGATTTGGAGGCCAATCACTGCCACCTTTTATTTCCCTGTGG GTCCAGGAACTGGATTTCTTTATTTGGTCAATTTATATTTCTTATATCAGTATTCTACGCGA GATTTGCATCGTGATTACTGGCTTAGCAATGGATATGCAGTTGCTGATGATTCCTCTGATCA TGTCAGTACTTTATGTCTGGGCCCAGCTGAACAGAGACATGATTGTATCATTTTGGTTTGGA ACACGATTTAAGGCCTGCTATTTACCCTGGGTTATCCTTGGATTCAACTATATCATCGGAGG CTCGGTAATCAATGAGCTTATTGGAAATCTGGTTGGACATCTTTATTTTTTCCTAATGTTCA GATACCCAATGGACTTGGGAGGAAGAAATTTTCTATCCACACCTCAGTTTTTGTACCGCTGG CTGCCCAGTAGGAGAGGAGTATCAGGATTTGGTGTGCCCCCTGCTAGCATGAGGCGAGC TGCTGATCAGAATGGCGGAGGCGGGAGACACAACTGGGGCCAGGGCTTTCGACTTGGAGACC AGTGAAGGGGCGGCCTCGGGCAGCCGCTCCTCTCAAGCCACATTTCCTCCCAGTGCTGGGTG CACTTAACAACTGCGTTCTGGCTAACACTGTTGGACCTGACCCACACTGAATGTAGTCTTTC AGTACGAGACAAAGTTTCTTAAATCCCGAAGAAAAATATAAGTGTTCCACAAGTTTCACGAT TCTCATTCAAGTCCTTACTGCTGTGAAGAACAAATACCAACTGTGCAAAATTGCAAAACTGAC TACATTTTTTGGTGTCTTCTCTCTCCCCTTTCCGTCTGAATAATGGGTTTTAGCGGGTCCT AATCTGCTGGCATTGAGCTGGGGCTGGGTCACCAAACCCTTCCCAAAAGGACCTTATCTCTT TCTTGCACACATGCCTCTCTCCCACTTTTCCCAACCCCCACATTTGCAACTAGAAAAAGTTG ACAACAATCATATTCACGTTATTTTCCCCTTTTGGTGGCAGAACTGTTACCAATAGGGGGAG AAGACAGCCACGGATGAAGCGTTTCTCAGCTTTTGGAATTGCTTCGACTGACATCCGTTGTT AACCGTTTGCCACTCTTCAGATATTTTTTATAAAAAAAGTACCACTGAGTTCATGAGGGCCA TCAAGACTGTAGTGGAGTTGCAGCTAACATGGGTTAGGTTTAAACCATGGGGGATGCACCCC TTTGCGTTTCATATGTAGCCCTACTGGCTTTGTGTAGCTGGAGTAGTTGGGTTGCTTTGTGT TAGGAGGATCCAGATCATGTTGGCTACAGGGAGATGCTCTCTTTGAGAGGTCCTGGGCATTG ATTCCCATTTCAATCTCATTCTGGATATGTGTTCATTGAGTAAAGGAGGAGAGACCCTCATA GAGGAAGGCGCAGCTCCTCTCTGCACGTAGATCATTTTTTAAAGCTAATGTAAGCACATCTA AGGGAATAACATGATTTAAGGTTGAAATGGCTTTAGAATCATTTGGGTTTGAGGGTGTGTTA TTTTGAGTCATGAATGTACAAGCTCTGTGAATCAGACCAGCTTAAATACCCCACACCTTTTTT TCGTAGGTGGGCTTTTCCTATCAGAGCTTGGCTCATAACCAAATAAAGTTTTTTGAAGGCCA TGGCTTTTCACACAGTTATTTTATTTTATGACGTTATCTGAAAGCAGACTGTTAGGAGCAGT ATTGAGTGGCTGTCACACTTTGAGGCAACTAAAAAGGCTTCAAACGTTTTGATCAGTTTCTT TTCAGGAAACATTGTGCTCTAACAGTATGACTATTCTTTCCCCCACTCTTAAACAGTGTGAT GTGTGTTATCCTAGGAAATGAGAGTTGGCAAACAACTTCTCATTTTGAATAGAGTTTGTGTG TACTTCTCCATATTTAATTTATATGATAAAATAGGTGGGGAGAGTCTGAACCTTAACTGTCA TGTTTTGTTGTTCATCTGTGGCCACAATAAAGTTTACTTGTAAAATTTTAGAGGCCATTACT CAGTCATTTTTCCTAAAGGTTTACAAGTATTTAGAACTTTTCAGTTCAGGGCAAAATGTTC ATGAAGTTATTCCTCTTAAACATGGTTAGGAAGCTGATGACGTTATTGATTTTGTCTGGATT ATGTTTCTGGAATAATTTTACCAAAACAAGCTATTTGAGTTTTGACTTGACAAGGCAAAACA TGACAGTGGATTCTCTTTACAAATGGAAAAAAAAAATCCTTATTTTGTATAAAGGACTTCCC TTTTTGTAAACTAATCCTTTTTATTGGTAAAAATTGTAAAATTAAAATGTGCAACTTG

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FIGURE 4

MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGLISPAYLFLWPEAFLYRFQIWRPITATFYF PVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNWICIVITGLAMDMQLLMIP LIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIGGSVINELIGNLVGHLYFFL MFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGGRHNWGQGFRLGDQ

FIGURE 5

GGGGCCGCGTCTAGGGCCGCTACGTGTTGTCCATAGCGACCATTTTGCATTAACTGGTTG GTAGCTTCTATCCTGGGGGCTGAGCGACTGCGGGCCAGCTCTTCCCCTACTCCCTCTCGGCT ${\tt CCTTGTGGCCCAAAGGCCTAACCGGGGTCCGGCGGTCTGGCCTAGGGATCTTCCCCGTTGCC}$ ${\tt CCTTTGGGGCGGGATGGCTGGAAGAAGAAGAAGAAGACGAGGTGGAGTGGGTAGTGGAGAGCATCG}$ $\tt CGGGGTTCCTGCGAGGCCCAGACTGGTCCATCCCCATCTTGGACTTTGTGGAACAGAAATGT$ GAAGTTAACTGCAAAGGAGGGCATGTGATAACTCCAGGAAGCCCAGAGCCGGTGATTTTGGT GGCCTGTGTTCCCCCTTGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGATTC ATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAATT AATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAGGC CATTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCCAGA AAAACATTGAAATGCAGCTGCAAGCCATTCGAATAATTCAAGAGAGAAATGGTGTATTACCT GACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAATCCT GAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAAGAAGAAAGGAAGAAGAAAA AACAGTTATCAGAGGCTAAAACAGAAGAGCCCACAGTGCATTCCAGTGAAGCTGCAATAATG CACAAAAAGGCCTGAAGATTCCTGGCTTAGAGCATGCGAGCATTGAAGGACCAATAGCAAAC TTATCAGTACTTGGAACAGAAGAACTTCGGCAACGAGAACACTATCTCAAGCAGAAGAGAGA TAAGTTGATGTCCATGAGAAAGGATATGAGGACTAAACAGATACAAAATATGGAGCAGAAAG GAAAACCCACTGGGGAGGTAGAGGAAATGACAGAGAAACCAGAAATGACAGCAGAGGAGAAG ${\tt CAAACATTACTAAAGAGGGGGGGTTGCTTGCAGGGGAGAACTCAAAGAAGAAGTTATTAATAAG\underline{\bf TA}}$ **CTTACACTG**

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FIGURE 6

MAAEEEDEVEWVVESIAGFLRGPDWSIPILDFVEQKCEVNCKGGHVITPGSPEPVILVACVP LVFDDEEESKLTYTEIHQEYKELVEKLLEGYLKEIGINEDQFQEACTSPLAKTHTSQAILQP VLAAEDFTIFKAMMVQKNIEMQLQAIRIIQERNGVLPDCLTDGSDVVSDLEHEEMKILREVL RKSKEEYDQEEERKRKKQLSEAKTEEPTVHSSEAAIMNNSQGDGEHFAHPPSEVKMHFANQS IEPLGRKVERSETSSLPQKGLKIPGLEHASIEGPIANLSVLGTEELRQREHYLKQKRDKLMS MRKDMRTKQIQNMEQKGKPTGEVEEMTEKPEMTAEEKQTLLKRRLLAEKLKEEVINK WO 99/63088

FIGURE 7

GGGCACAGCACATGTGAAGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGAT TCATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAA TTAATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAG ${\tt GCCATTTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCC}$ ${\tt AGAAAACATTGAAATGCAGCTGCAAGCCATTCGAATAATTCAAGAGAGAAATGGTGTATTA}$ ${\tt CCTGACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAAT}$ CCTGAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAA

GCGTGGTTTTTGTTCTGCAATAGGCGGCTTAGAGGGGGGGCTTTTTCGCCTATACCTACTG TAGCTTCTCCACGTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTG AGTGGAATGGAAAAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCAACAATGTATAC ATTCCTGCTAGGTGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATT CTGCCAATGAAGAAACAAGTATGATTATCTTCCAACTACTGTGAATGTGTGCTCAGAACTG AAATTTGAAATATGCTTCCTGGAAGGAATTCTCTGATTTCATGAAGTGGTCCATTCCTGCCT TTCTTTATTTCCTGGATAACTTGATTGTCTTCTATGTCCTGTCCTATCTTCAACCAGCCATG GCTGTTATCTTCTCAAATTTTAGCATTATAACAACAGCTCTTCTATTCAGGATAGTGCTGAA GAGGCGTCTAAACTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTGTCTATTGTGGCCT TGACTGCCGGGACTAAAACTTTACAGCACAACTTGGCAGGACGTGGATTTCATCACGATGCC TACAGCAAAGGAATGGACTTTTCCTGAAGCTAAATGGAACACCACAGCCAGAGTTTTCAGTC ACATCCGTCTTGGCATGGCCATGTTCTTATTATAGTCCAGTGTTTTATTTCTTCAATGGCT <u>AATATCTATAATGAAAAGATACTGAAGGAGGGGAACCAGCTCACTGAAAGCATCTTCATACA</u> GAACAGCAAACTCTATTTCTTTGGCATTCTGTTTAATGGGCTGACTCTGGGCCTTCAGAGGA GTAACCGTGATCAGATTAAGAACTGTGGATTTTTTTATGGCCACAGTGCATTTTCAGTAGCC CTTATTTTTGTAACTGCATTCCAGGGCCTTTCAGTGGCTTTCATTCTGAAGTTCCTGGATAA TCTTTGACTTCAGGCCCTCCCTGGAATTTTTCTTGGAAGCCCCATCAGTCCTTCTCTCTATA TTTATTTATAATGCCAGCAAGCCTCAAGTTCCGGAATACGCACCTAGGCAAGAAAGGATCCG AGATCTAAGTGGCAATCTTTGGGAGCGTTCCAGTGGGGATGGAGAAGAACTAGAAAGACTTA CCAAACCCAAGAGTGATGAGTCAGATGAAGATACTTTC<u>TAA</u>CTGGTACCCACATAGTTTGCA GCTCTCTTGAACCTTATTTTCACATTTTCAGTGTTTTGTAATATTTATCTTTTCACTTTGATA AACCAGAAATGTTTCTAAATCCTAATATTCTTTGCATATATCTAGCTACTCCCTAAATGGTT CCATCCAAGGCTTAGAGTACCCAAAGGCTAAGAAATTCTAAAGAACTGATACAGGAGTAACA ATATGAAGAATTCATTAATATCTCAGTACTTGATAAATCAGAAAGTTATATGTGCAGATTAT TTTCCTTGGCCTTCAAGCTTCCAAAAAACTTGTAATAATCATGTTAGCTATAGCTTGTATAT ACACATAGAGATCAATTTGCCAAATATTCACAATCATGTAGTTCTAGTTTACATGCCAAAGT CTTCCCTTTTTAACATTATAAAAGCTAGGTTGTCTCTTGAATTTTGAGGCCCTAGAGATAGT CTGGCCATACCATAGATTTGGGATGATGTAGTCTGTGCTAAATATTTTGCTGAAGAAGCAGT TTCTCAGACACATCTCAGAATTTTAATTTTTAGAAATTCATGGGAAATTGGATTTTTGT AATAATCTTTTGATGTTTTAAACATTGGTTCCCTAGTCACCATAGTTACCACTTGTATTTTA AGTCATTTAAACAAGCCACGGTGGGGCTTTTTTCTCCTCAGTTTGAGGAGAAAAATCTTGAT AATTCAAGCTGTGACTATTGTATATCTTTCCAAGAGTTGAAATGCTGGCTTCAGAATCATAC CAGATTGTCAGTGAAGCTGATGCCTAGGAACTTTTAAAGGGATCCTTTCAAAAGGATCACTT AGCAAACACATGTTGACTTTTAACTGATGTATGAATATTAATACTCTAAAAATAGAAAGACC AGTAATATAAGTCACTTTACAGTGCTACTTCACACTTAAAAGTGCATGGTATTTTTCATG GTATTTTGCATGCAGCCAGTTAACTCTCGTAGATAGAGAAGTCAGGTGATAGATGATATTAA AAATTAGCAAACAAAAGTGACTTGCTCAGGGTCATGCAGCTGGGTGATGATAGAAGAGTGGG CTTTAACTGGCAGGCCTGTATGTTTACAGACTACCATACTGTAAATATGAGCTTTATGGTGT CATTCTCAGAAACTTATACATTTCTGCTCTCCTTTCTCCTAAGTTTCATGCAGATGAATATA AGGTAATATACTATTATATAATTCATTTGTGATATCCACAATAATATGACTGGCAAGAATTG GTGGAAATTTGTAATTAAAATAATTATTAAACCT

MEKQCCSHPVICSLSTMYTFLLGAIFIALSSSRILLVKYSANEENKYDYLPTTVNVCSELVK LVFCVLVSFCVIKKDHQSRNLKYASWKEFSDFMKWSIPAFLYFLDNLIVFYVLSYLQPAMAV IFSNFSIITTALLFRIVLKRRLNWIQWASLLTLFLSIVALTAGTKTLQHNLAGRGFHHDAFF SPSNSCLLFRSECPRKDNCTAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISSMANI YNEKILKEGNQLTESIFIQNSKLYFFGILFNGLTLGLQRSNRDQIKNCGFFYGHSAFSVALI FVTAFQGLSVAFILKFLDNMFHVLMAQVTTVIITTVSVLVFDFRPSLEFFLEAPSVLLSIFI YNASKPOVPEYAPRQERIRDLSGNLWERSSGDGEELERLTKPKSDESDEDTF

FIGURE 11

CGGACGCGTGGGCGGACGCGTGGGCGGCCGGCTTGGCTAGCGCGCGGCGCCC GTGGCTAAGGCTGCTACGAAGCGAGCTTGGGAGGAGCAGCGCCTGCGGGGCAGAGGAGCAT CCCGTCTACCAGGTCCCAAGCGGCGTGGCCCGCGGGTCATGGCCAAAGGAGAAGGCGCCGAG AGCGGCTCCGCGGGGGCTGCTACCCACCAGCATCCTCCAAAGCACTGAACGCCCGGCCCA GGTGAAGAAGAACCGAAAAAGAAGAACAACAGTTGTCTGTTTGCAACAAGCTTTGCTATG CTATTGGATGTGGCTCAGGTGGGCCCTTTCTCTGCCTCCATCATCCTGTTTGTGGGCCGAGC CTGGGATGCCATCACAGACCCCCTGGTGGGCCTCTGCATCAGCAAATCCCCCTGGACCTGCC TGGGTCGCCTTATGCCCTGGATCATCTTCTCCACGCCCCTGGCCGTCATTGCCTACTTCCTC ATCTGGTTCGTGCCCGACTTCCCACACGGCCAGACCTATTGGTACCTGCTTTTCTATTGCCT CTTTGAAACAATGGTCACGTGTTTCCATGTTCCCTACTCGGCTCTCACCATGTTCATCAGCA ACCGAGCAGACTGAGCGGGATTCTGCCACCGCCTATCGGATGACTGTGGAAGTGCTGGGCAC AGTGCTGGGCACGGCGATCCAGGGACAAATCGTGGGCCAAGCAGACACGCCTTGTTTCCAGG ACTTCAATAGCTCTACAGTAGCTTCACAAAGTGCCAACCATACACATGGCACCACTTCACAC AGGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTG TGCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAGACCCTATGAAGCCCAGCAGTCTG AGCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACTT ATTACTGGCTTCCTCTCACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACTTTGTCTTGTT TTGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCT CGGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGCAAGAAGACAGCT GTATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAA ${\tt CCTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTAC}$ TACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCAT GGAACCGAGCCCATCTTCTTCTCTTCTATGTCTTCTTCACCAAGTTTGCCTCTGGAGTGTC ACTGGGCATTTCTACCCTCAGTCTGGACTTTGCAGGGTACCAGACCCGTGGCTGCTCGCAGC CGGAACGTGTCAAGTTTACACTGAACATGCTCGTGACCATGGCTCCCATAGTTCTCATCCTG CTGGGCCTGCTCTTCAAAATGTACCCCATTGATGAGGAGAGGCGGCGGCAGAATAAGAA GGCCCTGCAGGCACTGAGGGACGAGGCCAGCAGCTCTGGCTGCTCAGAAACAGACTCCACAG AGCTGGCTAGCATCCTCTAGGGCCCGCCACGTTGCCCGAAGCCACCATGCAGAAGGCCACAG AAGGGATCAGGACCTGTCTGCCGGCTTGCTGAGCAGCTGCAGGTGCTAGGAAGGGAA ${\tt CTGAAGACTCAAGGAGGTGGCCCAGGACACTTGCTGTGCTCACTGTGGGGCCGGCTGCTCTG}$ TGGCCTCCTGCCTCCCTCTGCCTGCCTGTGGGGCCAAGCCCTGGGGCCTGCCACTGTGAATA TTAATGTTATTAATTTTCATAAAAGCTGGAAAGC

MWLRWALSLPPSSCLWAEPGMPSQTPWWASASANPPGPAWVALCPGSSSPRPWPSLPTSSSG
SCPTSHTARPIGTCFSIASLKQWSRVSMFPTRLSPCSSATEQTERDSATAYRMTVEVLGTVL
GTAIQGQIVGQADTPCFQDFNSSTVASQSANHTHGTTSHRETQKAYLLAAGVIVCIYIICAV
ILILGVREQREPYEAQQSEPIAYFRGLRLVMSHGPYIKLITGFLFTSLAFMLVEGNFVLFCT
YTLGFRNEFQNLLLAIMLSATLTIPIWQWFLTRFGKKTAVYVGISSAVPFLILVALMESNLI
ITYAVAVAAGISVAAAFLLPWSMLPDVIDDFHLKQPHFHGTEPIFFSFYVFFTKFASGVSLG
ISTLSLDFAGYQTRGCSQPERVKFTLNMLVTMAPIVLILLGLLLFKMYPIDEERRRQNKKAL
QALRDEASSSGCSETDSTELASIL

GGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTGT
GCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAACCCTATGAAGCCCAGCAGTCTGA
GCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACTTA
TTACTGGCTTCCTCTTCACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACTTTGTCTTGTTT
TGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCTC
GGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGCAAGAAGACAGCTG
TATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCCATGGAGAGTAAC
CTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTACT
ACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCATG
GAACCGAGCCCAT

GGGGCTTCGCCCCAGCGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGT ATGAGCAGGTCTGAAGACTAACATTTTGTGAAGTTGTAAAACAGAAAACCTGTTAGAAATGT GGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAATTTGGACATCTGCTGCT TTCATATTTCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTTACCTTATAT CAGTGACACTGGTACAGTAGCTCCAGAAAAATGCTTATTTGGGGCAATGCTAAATATTGCGG CAGTTTTATGCATTGCTACCATTTATGTTCGTTATAAGCAAGTTCATGCTCTGAGTCCTGAA GAGAACGTTATCATCAAATTAAACAAGGCTGGCCTTGTACTTGGAATACTGAGTTGTTTAGG ACTTTCTATTGTGGCAAACTTCCAGAAAACAACCCTTTTTGCTGCACATGTAAGTGGAGCTG TGCTTACCTTTGGTATGGGCTCATTATATATGTTTGTTCAGACCATCCTTTCCTACCAAATG CAGCCCAAAATCCATGGCAAACAAGTCTTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGG AGTAAGTGCACTTAGCATGCTGACTTGCTCATCAGTTTTGCACAGTGGCAATTTTGGGACTG ATTTAGAACAGAAACTCCATTGGAACCCCGAGGACAAAGGTTATGTGCTTCACATGATCACT ACTGCAGCAGAATGGTCTATGTCATTTTCCTTCTTTTGGTTTTTTCCTGACTTACATTCGTGA TTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACATGGATTAACCCTCTATGACACTG CACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCCAGAGATATTTGATGAAAGGAT AAAATATTTCTGTAATGATTATGATTCTCAGGGGATTGGGGAAAGGTTCACAGAAGTTGCTTA TTCTTCTCTGAAATTTTCAACCACTTAATCAAGGCTGACAGTAACACTGATGAATGCTGATA ATCAGGAAACATGAAAGAAGCCATTTGATAGATTATTCTAAAGGATATCATCAAGAAGACTA TTAAAAACACCTATGCCTATACTTTTTTATCTCAGAAAATAAAGTCAAAAGACTATG

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FIGURE 15

MWWFQQGLSFLPSALVIWTSAAFIFSYITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNI
AAVLCIATIYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTTLFAAHVSG
AVLTFGMGSLYMFVQTILSYQMQPKIHGKQVFWIRLLLVIWCGVSALSMLTCSSVLHSGNFG
TDLEQKLHWNPEDKGYVLHMITTAAEWSMSFSFFGFFLTYIRDFQKISLRVEANLHGLTLYD
TAPCPINNERTRLLSRDI

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FIGURE 16

CCCACGCGTCCGCCGCCGCTGCGTCCCGGAGTGCAAGTGAGCTTCTCGGCTGCCCCGCGG $\tt CCGGGGTGCGGAGCCGAC{\color{red} \underline{ATG}} CGCCCGCTTCTCGGCCTCCTTCTGGTCTTCGCCGGCTGCAC$ AGGCTGGAGGCAGGTCGCTGTGGTTCCCCTCCGACCTGGCAGAGCTGCGGGAGCTCTCTGAG GTCCTTCGAGAGTACCGGAAGGAGCACCAGGCCTACGTGTTCCTGCTCTTCTGCGGCGCCCTA CCTCTACAAACAGGGCTTTGCCATCCCCGGCTCCAGCTTCCTGAATGTTTTAGCTGGTGCCT TGCTACCTGCTCCCAGTATTTTTGGCAAACAGTTGGTGGTGTCCTACTTTCCTGATAAAGT TGAGACTTTTCCCCATGACACCAAACTGGTTCTTGAACCTCTCGGCCCCAATTCTGAACATT CCCATCGTGCAGTTCTTCTCAGTTCTTATCGGTTTGATCCCATATAATTTCATCTGTGT GCAGACAGGGTCCATCCTGTCAACCCTAACCTCTCTGGATGCTCTTTTCTCCTGGACACTG TCTTTAAGCTGTTGGCCATTGCCATGGTGGCATTAATTCCTGGAACCCTCATTAAAAAATTT AGTCAGAAACATCTGCAATTGAATGAAACAAGTACTGCTAATCATATACACAGTAGAAAAGA CACATGATCTGGATTTTCTGTTTGCCACATCCCTGGACTCAGTTGCTTATTTGTGTAATGGA TGTGGTCCTCTAAAGCCCCTCATTGTTTTTGATTGCCTTCTATAGGTGATGTGGACACTGTG CATCAATGTGCAGTGTCTTTTCAGAAAGGACACTCTGCTCTTGAAGGTGTATTACATCAGGT TTTCAAACCAGCCCTGGTGTAGCAGACACTGCAACAGATGCCTCCTAGAAAATGCTGTTTGT GGCCGGCGCGCTGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCCGGTGATTC ACAAGGTCAGGAGTTCAAGACCAGCCTGGCCAAGATGGTGAAATCCTGTCTCTAATAAAAAT ACAAAAATTAGCCAGGCGTGGTGGCAGGCACCTGTAATCCCAGCTACTCGGGAGGCTGAGGC AGGAGAATTGCTTGAACCAAGGTGGCAGAGGTTGCAGTAAGCCAAGATCACACCACTGCACT CCAGCCTGGGTGATAGAGTGAGACACTGTCTTGAC

FIGURE 18

MRPLLGLLLVFAGCTFALYLLSTRLPRGRRLGSTEEAGGRSLWFPSDLAELRELSEVLREYR
KEHQAYVFLLFCGAYLYKQGFAIPGSSFLNVLAGALFGPWLGLLLCCVLTSVGATCCYLLSS
IFGKQLVVSYFPDKVALLQRKVEENRNSLFFFLLFLRLFPMTPNWFLNLSAPILNIPIVQFF
FSVLIGLIPYNFICVQTGSILSTLTSLDALFSWDTVFKLLAIAMVALIPGTLIKKFSQKHLQ
LNETSTANHIHSRKDT

CCGAGGCGGAGGAGCCCGAGGGGGGCGCGAGCCCCGCATGAATCATTGTAGTCAATCATTTT CCAGTTCTCAGCCGCTCAGTTGTGATCAAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAA TAGGAAAATAACTTGGGATTTTATATTGGAAGAC<u>ATG</u>GATCTTGCTGCCAACGAGATCAGCA TCAGAGAGGCAATTGAAAAATTTATCAGACAGCTGCTGGAAAAGAATGAACCTCAGAGACC CCCCCGCAGTATCCTCTCTTATAGTTGTGTATAAGGTTCTCGCAACCTTGGGATTAATCT TGCTCACTGCCTACTTTGTGATTCAACCTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTCT GGAGCTCACACCTGGCGCTCACTCATCCATCACATTAGGCTGATGTCCTTGCCCATTGCCAA CAGACTTTGACCCCTGGTGGACAAACGACTGTGAGCAGAATGAGTCAGAGCCCATTCCTGCC AACTGCACTGGCTGTGCCCAGAAACACCTGAAGGTGATGCTCCTGGAAGACGCCCCAAGGAA ATTTGAGAGGCTCCATCCACTGGTGATCAAGACGGGAAAGCCCCTGTTGGAGGAAGAGATTC AGCATTTTTTGTGCCAGTACCCTGAGGCGACAGAAGGCTTCTCTGAAGGGTTTTTCGCCAAG TGGTGGCGCTGCTTTCCTGAGCGGTGGTTCCCATTTCCTTATCCATGGAGGAGACCTCTGAA CCTCTTTAAACAAGTGCTCCTTTCTTCACCCAGAACCTGTTGTGGGGAGTAAGATGCATAAG GTGCCGAAGACATTGTCAGTCTGTGGCCATGCCAATAGAGCCAGGGGATATCGGCTATGTCG ACACCACCCACTGGAAGGTCTACGTTATAGCCAGAGGGGTCCAGCCTTTGGTCATCTGCGAT $\tt GGAACCGCTTTCTCAGAACTG\underline{TAG}GAAATAGAACTGTGCACAGGAACAGCTTCCAGAGCCGA$ AAACCAGGTTGAAAGGGGAAAAATAAAAACAAAAACGATGAAACTGCAAAAA

FIGURE 20

MDLAANEISIYDKLSETVDLVRQTGHQCGMSEKAIEKFIRQLLEKNEPQRPPPQYPLLIVVY
KVLATLGLILLTAYFVIQPFSPLAPEPVLSGAHTWRSLIHHIRLMSLPIAKKYMSENKGVPL
HGGDEDRPFPDFDPWWTNDCEQNESEPIPANCTGCAQKHLKVMLLEDAPRKFERLHPLVIKT
GKPLLEEEIQHFLCQYPEATEGFSEGFFAKWWRCFPERWFPFPYPWRRPLNRSQMLRELFPV
FTHLPFPKDASLNKCSFLHPEPVVGSKMHKMPDLFIIGSGEAMLQLIPPFQCRRHCQSVAMP
IEPGDIGYVDTTHWKVYVIARGVQPLVICDGTAFSEL

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FIGURE 22

CCCACGCGTCCGCCCACGCGTCCGGCTGAACACCTCTTCTTTGGAGTCAGCCACTGATGAGG CTCCCTGCCACCACTATGGCAGCCCCACCTTCTTTGAAGACTTCCAGGCTTTTTGTGCCA CACCCGAATGGCGCCACTTCATCGACAACAGGTACAGCCAACCATGTCCCAGTTCGAAATG GACACGTATGCTAAGAGCCACGACCTTATGTCAGGTTTCTGGAATGCCTGCTATGACATGCT TATGAGCAGTGGGCAGCGCCCAGTGGGAGCGCCCCAGAGTCGTCGGGCCTTCCAGGAGC TGGTGCTGGAACCTGCGCAGAGGCGGCGCGCCTGGAGGGGCTACGCTACACGGCAGTGCTG AAGCAGCAGCAACGCAGCACTCCATGGCCCTGCTGCACTGGGGGGGCGCTGTGGCGCCAGCT CGCCAGCCCATGTGGGGCCTGGGGGGGGACACTCCCATCCCCGCTGGAAACTGTCCA GCGCCGAGACATATTCACGCATGCGTCTGAAGCTGGTGCCCAACCATCACTTCGACCCTCAC CTCACTGCCTCTGGCAGTGACCAAAGAGGCCAAAGTGAGCACCCCACCCGAGTTGCTGCAGG AGGACCAGCTCGGCGAGGACGAGCTGGCTGAGCTGGAGACCCCGATGGAGGCAGCAGAACTG GATGAGCAGCGTGAGAAGCTGGTGCTGTCGGCCGAGTGCCAGCTGGTGACGGTAGTGGCCGT GGTCCCAGGGCTGCTGGAGGTCACCACACAGAATGTATACTTCTACGATGGCAGCACTGAGC GCGTGGAAACCGAGGAGGGCATCGGCTATGATTTCCGGCGCCCACTGGCCCAGCTGCGTGAG GTCCACCTGCGGCGTTTCAACCTGCGCCGTTCAGCACTTGAGCTCTTCTTTATCGATCAGGC CAACTACTTCCTCAACTTCCCATGCAAGGTGGGCACGACCCCAGTCTCATCTCCTAGCCAGA CTCCGAGACCCCAGCCTGGCCCCATCCCACCCCATACCCAGGTACGGAACCAGGTGTACTCG TGGCTCCTGCGCCTACGGCCCCCCTCTCAAGGCTACCTAAGCAGCCGCTCCCCCAGGAGAT GCTGCGTGCCTCAGGCCTTACCCAGAAATGGGTACAGCGTGAGATATCCAACTTCGAGTACT TGATGCAACTCAACACCATTGCGGGGCGGACCTACAATGACCTGTCTCAGTACCCTGTGTTC CCCTGGGTCCTGCAGGACTACGTGTCCCCAACCCTGGACCTCAGCAACCCAGCCGTCTTCCG GGACCTGTCTAAGCCCATCGGTGTGGTGAACCCCAAGCATGCCCAGCTCGTGAGGGAGAAGT ATGAAAGCTTTGAGGACCCAGCAGGGACCATTGACAAGTTCCACTATGGCACCCACTACTCC AATGCAGCAGGCGTGATGCACTACCTCATCCGCGTGGAGCCCTTCACCTCCCTGCACGTCCA GCTGCAAAGTGGCCGCTTTGACTGCTCCGACCGGCAGTTCCACTCGGTGGCGGCAGCCTGGC AGGCACGCCTGGAGAGCCCTGCCGATGTGAAGGAGCTCATCCCGGAATTCTTCTACTTTCCT GACTTCCTGGAGAACCAGAACGGTTTTGACCTGGGCTGTCTCCAGCTGACCAACGAGAAGGT AGGCGATGTGGTGCTACCCCCGTGGGCCAGCTCTCCTGAGGACTTCATCCAGCAGCACCGCC AGGCTCTGGAGTCGGAGTATGTGTCTGCACACCTACACGAGTGGATCGACCTCATCTTTGGC GGGGGCTGTAGACCTGGACCATGTGACAGATGAGCGGGAACGGAAGGCTCTGGAGGGCATTA TCAGCAACTTTGGGCAGACTCCCTGTCAGCTGCTGAAGGAGCCACATCCAACTCGGCTCTCA GCTGAGGAAGCAGCCCATCGCCTTGCACGCCTGGACACTAACTCACCTAGCATCTTCCAGCA CCTGGACGAACTCAAGGCATTCTTCGCAGAGGTGACTGTGAGTGCCAGTGGGCTGCTGGGCA CCCACAGCTGGTTGCCCTATGACCGCAACATAAGCAACTACTTCAGCTTCAGCAAAGACCCC ACCATGGGCAGCCACAGAGCGACTGCTGAGTGGCCCGTGGGTGCCAGGCAGTGGTGT GAGTGGACAAGCACTGGCAGTGGCCCCGGATGGAAAGCTGCTATTCAGCGGTGGCCACTGGG ATGGCAGCCTGCGGGTGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGCTGCCAC CTTGATGTAGTAACCTGCCTTGCACTGGACACCTGTGGCATCTACCTCATCTCAGGCTCCCG CAAAGCCTGTGCAGGTCCTGTATGGGCATGGGGCTGCAGTGAGCTGTGTGGCCCATCAGCACT GAACTTGACATGGCTGTCTGGATCTGAGGATGGAACTGTGATCATACACACTGTACGCCG ${\tt CGGACAGTTGTAGCGGCACTACGGCCTCTGGGTGCCACATTCCCTGGACCTATTTTCCACC}$ CAGGTCACCTACTCCTTGCACCTGTATTCAGTCAATGGGAAGTTGCGGGCTTCACTGCCCCT GGCAGAGCAGCCTACAGCCCTGACGGTGACAGAGGACTTTGTGTTGCTGGGCACCGCCCAGT GCGCCCTGCACATCCTCCAACTAAACACACTGCTCCCGGCCGCCCCCCTTGCCCATGAAG GTGGCCATCCGCAGCGTGGCCGTGACCAAGGAGCGCAGCCACGTGCTGGTGGGCCTGGAGGA TGGCAAGCTCATCGTGGTGGTCGCGGGGCAGCCCTCTGAGGTGCGCAGCAGCCAGTTCGCGC GGAAGCTGTGGCGGTCCTCGCGGCGCATCTCCCAGGTGTCCTCGGGAGAGACGGAATACAAC ${\tt CCTACTGAGGCGCGC\underline{TGA}} {\tt ACCTGGCCAGTCCGGCTGCTCGGGCCCCGGCCGGCAGGCCTG}$ GCCCGGGAGGCCCCGCCCAGAAGTCGGCGGGAACACCCCGGGGTGGGCAGCCCAGGGGGTGA GCGGGGCCCACCCTGCCCAGCTCAGGGATTGGCGGGCGATGTTACCCCCTCAGGGATTGGCG GGCGGAAGTCCCGCCCTCGCCGGCTGAGGGGCCCCTGAGGGCCAGCACTGGCGTCT

FIGURE 23

MSQFEMDTYAKSHDLMSGFWNACYDMLMSSGQRRQWERAQSRRAFOELVLEPAORRARLEGL RYTAVLKQQATQHSMALLHWGALWRQLASPCGAWALRDTPIPRWKLSSAETYSRMRLKLVPN HHFDPHLEASALRDNLGEVPLTPTEEASLPLAVTKEAKVSTPPELLOEDOLGEDELAELETP MEAAELDEQREKLVLSAECQLVTVVAVVPGLLEVTTQNVYFYDGSTERVETEEGIGYDFRRP LAQLREVHLRRFNLRRSALELFFIDQANYFLNFPCKVGTTPVSSPSQTPRPQPGPIPPHTQV RNQVYSWLLRLRPPSQGYLSSRSPQEMLRASGLTQKWVQREISNFEYLMQLNTIAGRTYNDL SOYPVFPWVLODYVSPTLDLSNPAVFRDLSKPIGVVNPKHAOLVREKYESFEDPAGTIDKFH YGTHYSNAAGVMHYLIRVEPFTSLHVQLQSGRFDCSDROFHSVAAAWOARLESPADVKELIP EFFYFPDFLENQNGFDLGCLQLTNEKVGDVVLPPWASSPEDFIQQHRQALESEYVSAHLHEW IDLIFGYKQRGPAAEEALNVFYYCTYEGAVDLDHVTDERERKALEGIISNFGQTPCQLLKEP HPTRLSAEEAAHRLARLDTNSPSIFOHLDELKAFFAEVTVSASGLLGTHSWLPYDRNISNYF SFSKDPTMGSHKTQRLLSGPWVPGSGVSGQALAVAPDGKLLFSGGHWDGSLRVTALPRGKLL SQLSCHLDVVTCLALDTCGIYLISGSRDTTCMVWRLLHQGGLSVGLAPKPVQVLYGHGAAVS CVAISTELDMAVSGSEDGTVIIHTVRRGOFVAALRPLGATFPGPIFHLALGSEGOIVVOSSA WERPGAQVTYSLHLYSVNGKLRASLPLAEQPTALTVTEDFVLLGTAOCALHILOLNTLLPAA PPLPMKVAIRSVAVTKERSHVLVGLEDGKLIVVVAGOPSEVRSSOFARKLWRSSRRISOVSS GETEYNPTEAR

CACGGCCCACCTTGTGAACTCCTCGTGCCCAGGGCTGATGTGCGTCTTCCAGGGCTACTCAT CCAAAGGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCCTGGGGCTCTTC TGGACCCTTAACTGGGTACTGGCCCTGGGCCAATGCGTCCTCGCTGGAGCCTTTGCCTCCTT CTACTGGGCCTTCCACAAGCCCCAGGACATCCCTACCTTCCCCTTAATCTCTGCCTTCATCC GCACACTCCGTTACCACACTGGGTCATTGGCATTTGGAGCCCTCATCCTGACCCTTGTGCAG ATAGCCCGGGTCATCTTGGAGTATATTGACCACAAGCTCAGAGGAGTGCAGAACCCTGTAGC CCGCTGCATCATGTGCTGTTTCAAGTGCTGCCTCTGGTGTCTGGAAAAATTTATCAAGTTCC TAAACCGCAATGCATCATCATCATCGCCATCTACGGGAAGAATTTCTGTGTCTCAGCCAAA AATGCGTTCATGCTACTCATGCGAAACATTGTCAGGGTGGTCGTCCTGGACAAAGTCACAGA CCTGCTGCTGTTCTTTGGGAAGCTGCTGGTGGTGGTGGGGGGTCCTGTCCTTTTT TTTTCTCCGGTCGCATCCCGGGGCTGGGTAAAGACTTTAAGAGCCCCCCACCTCAACTATTAC TGGCTGCCCATCATGACCTCCATCCTGGGGGCCTATGTCATCGCCAGCGGCTTCTTCAGCGT TTTCGGCATGTGTGGACACGCTCTTCCTCTGCTTCCTGGAAGACCTGGAGCGGAACAACG GCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTTCTAAAGATTCTGGGCAAGAAGAAC GAGGCGCCCCGGACAACAAGAAGAGGAAGAAGTGACAGCTCCGGCCCTGATCCAGGACTGC ACCCCACCCCACCGTCCAGCCATCCAACCTCACTTCGCCTTACAGGTCTCCATTTTGTGGT AAAAAAAGGTTTTAGGCCAGGCGCCGTGGCTCACGCCTGTAATCCAACACTTTGAGAGGCTG AGGCGGCGGATCACCTGAGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCTCC GTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTCATCCCAGCTAC TCGGGAGGCTGAGGCAGAATCGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGA AAAGATTTTATTAAAGATATTTTGTTAACTC

FIGURE 25

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLGLF
WTLNWVLALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQ
IARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAK
NAFMLLMRNIVRVVVLDKVTDLLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY
WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYMSKSLLKILGKKN
EAPPDNKKRKK

FIGURE 26

GAGTCTTGACCGCCGCGGGCTCTTGGTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGT GGCTATGTTCGTGTCCGATTTCCGCAAAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCC CAGTGTGACCACGTGCAATATACGCTGGTTCCAGTTTCTGGGTGGCAAGAACTTGAAACTGC ATTTCTTGAGCATAAAGAACAGTTTCATTATTTTATTCTCATAAACTGTGGAGCTAATGTAG CCAGTCAATGTCATCAATGTATACAACGATACCCAGATCAAATTACTCATTAAACAAGATGA TGACCTTGAAGTTCCCGCCTATGAAGACATCTTCAGGGATGAAGAGGAGGATGAAGAGCATT CAGGAAATGACAGTGATGGGTCAGAGCCTTCTGAGAAGCGCACACGGTTAGAAGAGGAGATA GTGGAGCAAACCATGCGGAGGAGGCGGCGAGAGTGGGAGGCCCGGAGAAGAGACATCCT CTTTGACTACGAGCAGTATGAATATCATGGGACATCGTCAGCCATGGTGATGTTTGAGCTGG CTTGGATGCTGTCCAAGGACCTGAATGACATGCTGTGGTGGGCCATCGTTGGACTAACAGAC CAGTGGGTGCAAGACAAGATCACTCAAATGAAATACGTGACTGATGTTGGTGTCCTGCAGCG CCACGTTTCCCGCCACAACCACCGGAACGAGGATGAGGAGAACACTCTCCGTGGACTGCA CACGGATCTCCTTTGAGTATGACCTCCGCCTGGTGCTCTACCAGCACTGGTCCCTCCATGAC AGCCTGTGCAACACCAGCTATACCGCAGCCAGGTTCAAGCTGTGGTCTGTGCATGGACAGAA GCGGCTCCAGGAGTTCCTTGCAGACATGGGTCTTCCCCTGAAGCAGGTGAAGCAGAAGTTCC AGGCCATGGACATCTCCTTGAAGGAGAATTTGCGGGAAATGATTGAAGAGTCTGCAAATAAA TCTGGCCAGCGACGTGGTCTTTGCCACCATGTCTTTGATGGAGAGCCCCGAGAAGGATGGCT CAGGGACAGATCACTTCATCCAGGCTCTGGACAGCCTCTCCAGGAGTAACCTGGACAAGCTG TACCATGGCCTGGAACTCGCCAAGAAGCAGCTGCGAGCCACCCAGCAGACCATTGCCAGCTGC CTTTGCACCAACCTCGTCATCTCCCAGGGGCCTTTCCTGTACTGCTCTCTCATGGAGGGCAC TCCAGATGTCATGCTGTTCTCTAGGCCGGCATCCCTAAGCCTGCTCAGCAAACACCTGCTCA AGTCCTTTGTGTGTTCGACAAAGAACCGGCGCTGCAAACTGCTGCCCCTGGTGATGGCTGCC CCCTGAGCATGGAGCATGGCACAGTGACCGTGGTGGGCATCCCCCCAGAGACCGACAGCTC GGACAGGAAGAACTTTTTTGGGAGGGCGTTTGAGAAGGCAGCGGAAAGCACCAGCTCCCGGA TGCTGCACAACCATTTTGACCTCTCAGTAATTGAGCTGAAAGCTGAGGATCGGAGCAAGTTT CTGGACGCACTTATTTCCCTCCTGTCCTAGGAATTTGATTCTTCCAGAATGACCTTCTTATT TATGTAACTGGCTTTCATTTAGATTGTAAGTTATGGACATGATTTGAGATGTAGAAGCCATT TTTTATTAAATAAAATGCTTATTTTAGGAAA

FIGURE 27

MFVSDFRKEFYEVVQSQRVLLFVASDVDALCACKILQALFQCDHVQYTLVPVSGWQELETAF
LEHKEQFHYFILINCGANVDLLDILQPDEDTIFFVCDSHRPVNVVNVYNDTQIKLLIKQDDD
LEVPAYEDIFRDEEEDEEHSGNDSDGSEPSEKRTRLEEEIVEQTMRRRQRREWEARRRDILF
DYEQYEYHGTSSAMVMFELAWMLSKDLNDMLWWAIVGLTDQWVQDKITQMKYVTDVGVLQRH
VSRHNHRNEDEENTLSVDCTRISFEYDLRLVLYQHWSLHDSLCNTSYTAARFKLWSVHGQKR
LQEFLADMGLPLKQVKQKFQAMDISLKENLREMIEESANKFGMKDMRVQTFSIHFGFKHKFL
ASDVVFATMSLMESPEKDGSGTDHFIQALDSLSRSNLDKLYHGLELAKKQLRATQQTIASCL
CTNLVISQGPFLYCSLMEGTPDVMLFSRPASLSLLSKHLLKSFVCSTKNRRCKLLPLVMAAP
LSMEHGTVTVVGIPPETDSSDRKNFFGRAFEKAAESTSSRMLHNHFDLSVIELKAEDRSKFL
DALISLLS

FIGURE 28

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FIGURE 29

CAGGAACCCTCTCTTTGGGTCTGGATTGGGACCCCTTTCCAGTACCATTTTTTCTAGTGAAC CACGAAGGGACGATACCAGAAAACACCCTCAACCCAAAGGAAATAGACTACAGCCCCAATTG GTCTTCCCTTTATCGAGTCAAGAAACCCCCCCTTCTTGAGCTATTTACAGCTTTTAACAATT GAGTAAAGTACGCTCCGGTCACC<u>ATG</u>GTGACAGCCGCCCTGGGTCCCGTCTGGGCAGCGCTC CTGCTCTTTCTCCTGATGTGAGATCCGTATGGTGGAGCTCACCTTTGACAGAGCTGTGGC CAGCGGCTGCCAACGGTGCTGTGACTCTGAGGACCCCCTGGATCCTGCCCATGTATCCTCAG CCTCTTCCTCCGGCCGCCCCACGCCCTGCCTGAGATCAGACCCTACATTAATATCACCATC TCCCCAAGGGGAGCCTGGCCCTCAGGGCAGCAAGGGTGACAAGGGGGAGATGGGCAGCCCCG GCGCCCGTGCCAGAAGCGCTTCTTCGCCTTCTCAGTGGGCCGCAAGACGGCCCTGCACAGC GGCGAGGACTTCCAGACGCTGCTCTTCGAAAGGGTCTTTGTGAACCTTGATGGGTGCTTTGA CATGGCGACCGGCCAGTTTGCTGCTCCCCTGCGTGGCATCTACTTCTTCAGCCTCAATGTGC ACAGCTGGAATTACAAGGAGACGTACGTGCACATTATGCATAACCAGAAAGAGGCTGTCATC CTGTACGCGCAGCCCAGCGAGCGCAGCATCATGCAGAGCCAGAGTGTGATGCTGGACCTGGC CTACGGGGACCGCGTCTGGGTGCGGCTCTTCAAGCGCCAGCGCGAGAACGCCATCTACAGCA ${\tt ACGACTTCGACACCTACATCACCTTCAGCGGCCACCTCATCAAGGCCGAGGACGAC\underline{TGA}GGG}$ CCTCTGGGCCACCCTCCGGCTGGAGAGCTCAGGTGCTGGTCCCGTCCCCTGCAGGGCTCAG TTTGCACTGCTGTGAAGCAGGAAGGCCAGGGAGGTCCCCGGGGACCTGGCATTCTGGGGAGA TGGACCTATTTTAAGAAGCTTGCTAACCTAAATATTCTAGAACTTTCCCAGCCTCGTAGCCC AGCACTTCTCAAACTTGGAAATGCATGCGAATCACCCGGGGTTCGTGTTAAATGCAGATTCT GACTCAGCAGGTCTGAGTGGGTCCAGGATTCTGTGTTTCTCATATGTTCCTGGGTGATGCTG ATGGGGTCAGTCTATGAACCACACTGGAGCAACCAGGTTCTAGGACTTTCTCAATATTCTAG TGAGACAGAGTCTTGCTCTGTTGCCCAGGCTAGAGTGCAGTGGTGCAATCTCAGTTCACTGC AACCTCTGCCTCCCGGGTTCAAGCGATTCTTCTGCCTCAGCCTCCCTAGTGGCTGGGATTAC AGGCGCCTGCTACCATGCCTGGCTAATTTTTTGTATTTTTAGTAGAGATGGGGTTTCACCATA GCTGGGATTACAGGTGTGAGCCACCGTGCCTGGCCAATTCCAACATTCTTAAATTCTCTCAT CCCTCCAGGGCTCCCCGTGCTATGTTCTCTTTACCCCTTCCCCCTCTTCTCTTGCTCAGGCC GGGTCCCGGGAAGGGTGAGGGGGTCAGACACAGGCCCTGCCCTGCCCTCAGTGACTGGCCA GTCCAGCCCAGGCGGGAGAGATGTGTACATAGGTTTTAAAGCAGACCCAGAGCTCATGGGG GCCTGTGTTCTGGGTGTTCAGGTGCTGCTGGTCCTCCATTACCCACTGCTCCCCAAGGCTGG TGGGACGGGGTCCCGGTGGCAGGGCAGGTATCTCCTTCCCGTTCCTCATCCACCTGCCCAG TGCTCATCGTTACAGCAAACCCCAGGGGGCCTTGGCCAGGTCAAGGGTTCTGTGAGGAGAGG ACCCAGGAGTGTGGGGGCATTTGGGGGGGTGAAGTGGCCCCCGAAGAATGGAACCCACACCCA TAGCTCTCCCCACAGCTGATACGGCATCCTGCGAGAAGACCTGCCCTCCTCACTGGGATCCC CTTCCTGCCTCCCAGGGCTCTGCCAGGGCCTTGCTCAGTCCCTTCCACCAAAGTCATCT CTCTGCCCCTCATGCCCCTCTCACCGGCCCAGTGCCCCGACTCTCCAGGCTTTATCAAGGTG CTAAGGCCCGGGTGGGCAGCTCCTCGTCTCAGAGCCCTCCTCCGGCCTGGTGCTGCCTTTAC AAACACCTGCAGGAGAAGGGCCACGGAAGCCCCAGGCTTTAGAGCCCTCAGCAGGTCTGGGG AGCTAGAGCAAAGGAGGGACCTCAGGCCTTCCGTTTCTTCTTCCAGGGTGGGGTGGCCTGGT CCATTGGTGCTCATGCAGACTCTGGGGCTGAGGTGCCCCGGGGGGTGATCTCTGGTGCTCAC AGCCGAGGGAGCCGTGGCTCATGGCCAGATGACGGAAACAGGGTCTGACCAAGTGCCAGGA

FIGURE 30

MVTAALGPVWAALLLFLLMCEIRMVELTFDRAVASGCQRCCDSEDPLDPAHVSSASSSGRPH
ALPEIRPYINITILKGDKGDPGPMGLPGYMGREGPQGEPGPQGSKGDKGEMGSPGAPCQKRF
FAFSVGRKTALHSGEDFQTLLFERVFVNLDGCFDMATGQFAAPLRGIYFFSLNVHSWNYKET
YVHIMHNQKEAVILYAQPSERSIMQSQSVMLDLAYGDRVWVRLFKRQRENAIYSNDFDTYIT
FSGHLIKAEDD

Important features:

Signal peptide:

amino acids 1-20'

N-glycosylation site.

amino acids 72-75

Clq domain proteins.

amino acids 144-178, 78-111 and 84-117

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FIGURE 31

ACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCCTCGGGCCCGACCCGCCAGGAAAGACTG ${\tt AGGCCGCGGCCTGCCCGGCTCCCTGCGCCGCCGCCTCCCGGGACAGAAG{\tt ATG}TG}$ CTCCAGGGTCCCTCTGCTGCTGCTGCTCCTGCTACTGGCCCTGGGGCCTGGGGTGCAGG GCTGCCCATCCGGCTGCCAGTGCAGCCACAGACAGTCTTCTGCACTGCCCGCCAGGGG ACCACGGTGCCCCGAGACGTGCCACCCGACACGGTGGGGCTGTACGTCTTTGAGAACGGCAT CACCATGCTCGACGCAGCCAGCTTTGCCGGCCTGCCGGGCCTGCAGCTCCTGGACCTGTCAC AGAACCAGATCGCCAGCCTGCCCAGCGGGGTCTTCCAGCCACTCGCCAACCTCAGCAACCTG GACCTGACGGCCAACAGGCTGCATGAAATCACCAATGAGACCTTCCGTGGCCTGCGGCGCCT CGAGCGCCTCTACCTGGGCAAGAACCGCATCCGCCACATCCAGCCTGGTGCCTTCGACACGC TCGACCGCCTCCTGGAGCTCAAGCTGCAGGACAACGAGCTGCGGGCACTGCCCCCGCTGCGC CTGCCCGCCTGCTGCTGCACCTCAGCCACAACAGCCTCCTGGCCCTGGAGCCCGGCAT CCTGGACACTGCCAACGTGGAGGCGCTGCGGCTGGTCTGGGGCTGCAGCAGCTGGACG AGGGGCTCTTCAGCCGCTTGCGCAACCTCCACGACCTGGATGTGTCCGACAACCAGCTGGAG TGAGCAACCTAAGCCTGCAGGCCCTGCCTGGCGACCTCTCGGGCCTCTTCCCCCGCCTGCGG $\tt CTGCTGGCAGCTGCCCGCAACCCCTTCAACTGCGTGTGCCCCCTGAGCTGGTTTGGCCCCTG$ GGTGCGCGAGAGCCACGTCACACTGGCCAGCCCTGAGGAGACGCGCTGCCACTTCCCGCCCA AGAACGCTGGCCGGCTGCTCCTGGAGCTTGACTACGCCGACTTTGGCTGCCCAGCCACCACC ACCACAGCCACAGTGCCCACCACGAGGCCCGTGGTGCGGGAGCCCACAGCCTTGTCTTCTAG CTGCCCCACCGACTGTAGGGCCTGTCCCCCAGCCCCAGGACTGCCCACCGTCCACCTGCCTC AATGGGGGCACATGCCACCTGGGGACACGGCACCACCTGGCGTGCTTGTGCCCCGAAGGCTT CACGGGCCTGTACTGTGAGAGCCAGATGGGGCAGGGGGACACGGCCCAGCCCTACACCAGTCA CGCCGAGGCCACCACGGTCCCTGACCCTGGGCATCGAGCCGGTGAGCCCCACCTCCCTGCGC GTGGGGCTGCAGCGCTACCTCCAGGGGGGGCTCCGTGCAGCTCAGGAGCCTCCGTCTCACCTA AGTACACGGTCACCCAGCTGCGGCCCAACGCCACTTACTCCGTCTGTGTCATGCCTTTGGGG CCCGGGCGGTGCCGAGGGCGAGGCCTGCGGGGAGGCCCATACACCCCCAGCCGTCCA CTCCAACCACGCCCAGTCACCCAGGCCCGCGAGGGCAACCTGCCGCTCCTCATTGCGCCCG CCCTGGCCGCGTGCTCCTGGCCGCGCTGCGGTGGGGGCAGCCTACTGTGTGCGGCGG GGGCGGCCATGGCAGCAGCGGCTCAGGACAAAGGGCAGGTGGGGCCAGGGGCCTGGGCCCCT GGAACTGGAGGGAGTGAAGGTCCCCTTGGAGCCAGGCCCGAAGGCAACAGAGGGCGGTGGAG AGGCCCTGCCCAGCGGGTCTGAGTGTGAGGTGCCACTCATGGGCTTCCCAGGGCCTGGCCTC ${\tt CAGTCACCCCTCCACGCAAAGCCCTACATC} {\color{red}{\textbf{TAA}}} {\tt GCCAGAGAGACAGGGCAGCTGGGGCCG}$ GGCTCTCAGCCAGTGAGATGGCCAGCCCCCTCCTGCTGCCACACCACGTAAGTTCTCAGTCC CAACCTCGGGGATGTGCAGACAGGGCTGTGTGACCACAGCTGGGCCCTGTTCCCTCTGGA CCTCGGTCTCCTCATCTGTGAGATGCTGTGGCCCAGCTGACGAGCCCTAACGTCCCCAGAAC CGAGTGCCTATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGGCG GGCCCTGCCATGTGCTAACGCATGCCTGGGTCCTGCGGCTCTCCCACTCCAGGCGGA CCCTGGGGGCCAGTGAAGGAAGCTCCCGGAAAGAGCAGAGGGGAGAGCGGGTAGGCGGCTGTG TGACTCTAGTCTTGGCCCCAGGAAGCGAAGGAACAAAAGAAACTGGAAAGGAAGATGCTTTA GGAACATGTTTTGCTTTTTTAAAATATATATATTTATAAGAGATCCTTTCCCATTTATTCTG GGAAGATGTTTTCAAACTCAGAGACAAGGACTTTGGTTTTTGTAAGACAAACGATGATATG AAGGCCTTTTGTAAGAAAAAATAAAAGATGAAGTGTGAAA

シシ /3へ0 **FIGURE 32**

MCSRVPLLLPLLLLALGPGVQGCPSGCQCSQPQTVFCTARQGTTVPRDVPPDTVGLYVFEN
GITMLDAGSFAGLPGLQLLDLSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETFRGLR
RLERLYLGKNRIRHIQPGAFDTLDRLLELKLQDNELRALPPLRLPRLLLLDLSHNSLLALEP
GILDTANVEALRLAGLGLQQLDEGLFSRLRNLHDLDVSDNQLERVPPVIRGLRGLTRLRLAG
NTRIAQLRPEDLAGLAALQELDVSNLSLQALPGDLSGLFPRLRLLAAARNPFNCVCPLSWFG
PWVRESHVTLASPEETRCHFPPKNAGRLLLELDYADFGCPATTTTATVPTTRPVVREPTALS
SSLAPTWLSPTAPATEAPSPPSTAPPTVGPVPQPQDCPPSTCLNGGTCHLGTRHHLACLCPE
GFTGLYCESQMGQGTRPSPTPVTPRPPRSLTLGIEPVSPTSLRVGLQRYLQGSSVQLRSLRL
TYRNLSGPDKRLVTLRLPASLAEYTVTQLRPNATYSVCVMPLGPGRVPEGEEACGEAHTPPA
VHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVRRGRAMAAAAQDKGQVGPGAG
PLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPGPGLQSPLHAKPYI

GAATCATCCACGCACCTGCAGCTCTGCTGAGAGAGTGCAAGCCGTGGGGGTTTTGAGCTCAT CTTCATCATTCATATGAGGAAATAAGTGGTAAAATCCTTGGAAATACA<u>ATG</u>AGACTCATCAG AAGAAAGGGAACTGATGACCAACTGCTCCAACATGTCTCTAAGAAAGGTTCCCGCAGACTTG ACCCCAGCCACACGACACTGGATTTATCCTATAACCTCCTTTTTCAACTCCAGAGTTCAGA TTTTCATTCTGTCTCCAAACTGAGAGTTTTGATTCTATGCCATAACAGAATTCAACAGCTGG **ATCTCAAAACCTTTGAATTCAACAAGGAGTTAAGATATTTAGATTTGTCTAATAACAGACTG** TGACACCATGCCTATCTGTGAGGAAGCTGGCAACATGTCACACCTGGAAATCCTAGGTTTGA GTGGGGCAAAAATACAAAAATCAGATTTCCAGAAAATTGCTCATCTGCATCTAAATACTGTC TTCTTAGGATTCAGAACTCTTCCTCATTATGAAGAAGGTAGCCTGCCCATCTTAAACACAAC **AAAACTGCACATTGTTTTACCAATGGACACAAATTTCTGGGTTCTTTTGCGTGATGGAATCA** AGACTTCAAAAATATTAGAAATGACAAATATAGATGGCAAAAGCCAATTTGTAAGTTATGAA **ATGCAACGAAATCTTAGTTTAGAAAATGCTAAGACATCGGTTCTATTGCTTAATAAAGTTGA** TTCAGATCCGAAATGTGACTTTTGGTGGTAAGGCTTATCTTGACCACAATTCATTTGACTAC TCAAATACTGTAATGAGAACTATAAAATTGGAGCATGTACATTTCAGAGTGTTTTACATTCA ACAGGATAAAATCTATTTGCTTTTGACCAAAATGGACATAGAAAACCTGACAATATCAAATG CACAAATGCCACACATGCTTTTCCCGAATTATCCTACGAAATTCCAATATTTAAATTTTGCC AATAATATCTTAACAGACGAGTTGTTTAAAAGAACTATCCAACTGCCTCACTTGAAAACTCT CATTTTGAATGGCAATAAACTGGAGACACTTTCTTTAGTAAGTTGCTTTGCTAACAACACAC CCTTGGAACACTTGGATCTGAGTCAAAATCTATTACAACATAAAAATGATGAAAAATTGCTCA TGGCCAGAAACTGTGGTCAATATGAATCTGTCATACAATAAATTGTCTGATTCTGTCTTCAG GTGCTTGCCCAAAAGTATTCAAATACTTGACCTAAATAATAACCAAATCCAAACTGTACCTA AAGAGACTATTCATCTGATGGCCTTACGAGAACTAAATATTGCATTTAATTTTCTAACTGAT CTCCCTGGATGCAGTCATTTCAGTAGACTTTCAGTTCTGAACATTGAAATGAACTTCATTCT CAGCCCATCTCTGGATTTTGTTCAGAGCTGCCAGGAAGTTAAAACTCTAAATGCGGGAAGAA ATGATGGTTGGATGGTCAGATTCATACACCTGTGAATACCCTTTAAACCTAAGGGGAACTAG GTTAAAAGACGTTCATCTCCACGAATTATCTTGCAACACACCTCTGTTGATTGTCACCATTG TGGTTATTATGCTAGTTCTGGGGTTGGCTGTGGCCTTCTGCTGTCTCCACTTTGATCTGCCC TGGTATCTCAGGATGCTAGGTCAATGCACAAACATGGCACAGGGTTAGGAAAACAACCCA CTTTATGAAAGCTACTTTGACCCTGGCAAAAGCATTAGTGAAAATATTGTAAGCTTCATTGA GAAAAGCTATAAGTCCATCTTTGTTTTGTCTCCCAACTTTGTCCAGAATGAGTGGTGCCATT ATGAATTCTACTTTGCCCACCACAATCTCTTCCATGAAAATTCTGATCATAATAATTCTTATC TTACTGGAACCCATTCCATTCTATTGCATTCCCACCAGGTATCATAAACTGAAAGCTCTCCT GGAAAAAAAGCATACTTGGAATGGCCCAAGGATAGGCGTAAATGTGGGCTTTTCTGGGCAA ACCTTCGAGCTGCTATTAATGTTAATGTATTAGCCACCAGAGAAATGTATGAACTGCAGACA TTCACAGAGTTAAATGAAGAGTCTCGAGGTTCTACAATCTCTCTGATGAGAACAGATTGTCT ATAAAATCCCACAGTCCTTGGGAAGTTGGGGACCACATACACTGTTGGGATGTACATTGATA CAACCTTTATGATGGCAATTTGACAATATTTATTAAAATAAAAAATGGTTATTCCCTTCATA TCAGTTTCTAGAAGGATTTCTAAGAATGTATCCTATAGAAACACCTTCACAAGTTTATAAGG GCTTATGGAAAAAGGTGTTCATCCCAGGATTGTTTATAATCATGAAAAATGTGGCCAGGTGC GAGATGGAGACCATCCTGGCCAACATGGTGAAACCCTGTCTCTACTAAAAATACAAAAATTA GCTGGGCGTGATGGTGCACGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATCG CTTGAACCCGGGAGGTGGCAGTTGCAGTGAGCTGAGATCGAGCCACTGCACTCCAGCCTGGT TCATGGCCACAAAATAAGGTCTAATTCAATAAATTATAGTACATTAATGTAATATAATATTA CATGCCACTAAAAAGAATAAGGTAGCTGTATATTTCCTGGTATGGAAAAAACATATTAATAT GTTATAAACTATTAGGTTGGTGCAAAACTAATTGTGGTTTTTTGCCATTGAAATGGCATTGAA ATAAAAGTGTAAAGAAATCTATACCAGATGTAGTAACAGTGGTTTGGGTCTGGGAGGTTGGA TTACAGGGAGCATTTGATTTCTATGTTGTGTATTTCTATAATGTTTGAATTGTTTAGAATGA ATCTGTATTCTTTTATAAGTAGAAAAAAAAAAAAGATAGTTTTTACAGCCT

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MRLIRNIYIFCSIVMTAEGDAPELPEERELMTNCSNMSLRKVPADLTPATTTLDLSYNLLFQ
LQSSDFHSVSKLRVLILCHNRIQQLDLKTFEFNKELRYLDLSNNRLKSVTWYLLAGLRYLDL
SFNDFDTMPICEEAGNMSHLEILGLSGAKIQKSDFQKIAHLHLNTVFLGFRTLPHYEEGSLP
ILNTTKLHIVLPMDTNFWVLLRDGIKTSKILEMTNIDGKSQFVSYEMQRNLSLENAKTSVLL
LNKVDLLWDDLFLILQFVWHTSVEHFQIRNVTFGGKAYLDHNSFDYSNTVMRTIKLEHVHFR
VFYIQQDKIYLLLTKMDIENLTISNAQMPHMLFPNYPTKFQYLNFANNILTDELFKRTIQLP
HLKTLILNGNKLETLSLVSCFANNTPLEHLDLSQNLLQHKNDENCSWPETVVNMNLSYNKLS
DSVFRCLPKSIQILDLNNNQIQTVPKETIHLMALRELNIAFNFLTDLPGCSHFSRLSVLNIE
MNFILSPSLDFVQSCQEVKTLNAGRNPFRCTCELKNFIQLETYSEVMMVGWSDSYTCEYPLN
LRGTRLKDVHLHELSCNTALLIVTIVVIMLVLGLAVAFCCLHFDLPWYLRMLGQCTQTWHRV
RKTTQEQLKRNVRFHAFISYSEHDSLWVKNELIPNLEKEDGSILICLYESYFDPGKSISENI
VSFIEKSYKSIFVLSPNFVQNEWCHYEFYFAHHNLFHENSDHIILILLEPIPFYCIPTRYHK
LKALLEKKAYLEWPKDRRKCGLFWANLRAAINVNVLATREMYELQTFTELNEESRGSTISLM

FIGURE 35A

GGGGGCTTTCTTGGGCTTGGCTTGGAACACCTGCCTCCAAGGACCGGCCTCGGAGGGGT CTGCGCGCCCTGTCCGCCCCGGCCCAGCCCAGCCCCGCGGGCCGGTCACACGCGCA GCCAGCCGGCCCCCCCGCGCCCCAAGCGCGCCCTCTGCTGTGCCCTTGCCCCCG CGCCAGCTTCTGCGCCCGCAGCCCGCCCGGCGCCCCCGGTGACCGTGACCCTGCCCTGGGCG $\tt CGGGGGGGAGCAGGC\underline{ATG}{\tt TCCCGCCCGGGGACCGCTACCCCAGCGCTGGCCCTGGTGCTCCT}$ GGCAGTGACCCTGGCCGGGGTCGGAGCCCAGGGCGCAGCCCTCGAGGACCCTGATTATTACG GGCAGGAGATCTGGAGCCGGGAGCCCTACTAĆGCGCGCGCGGAGCCCGAGCTCGAGACCTTC GCCCAAGAGGGCCACCAAGCCCCAAGAAGCTCCCCAAGAGGGGAGAAGTCGGCTCCGGAGCCGC CTCCACCAGGTAAACACAGCAACAAAAAAGTTATGAGAACCAAGAGCTCTGAGAAGGCTGCC TCTGGAAACCTTAAAAATCACAGACTTCCAGCTCCATGCCTCCACGGTGAAGCGCTATGGCC TGGGGGCACATCGAGGGAGACTCAACATCCAGGCGGGCATTAATGAAAATGATTTTTATGAC GGAGCGTGGTGCGCGGGAAGAAATGACCTCCAGCAGTGGATTGAAGTGGATGCTCGGCGCCT GACCAGATTCACTGGTGTCATCACTCAAGGGAGGAACTCCCTCTGGCTGAGTGACTGGGTGA CATCCTATAAGGTCATGGTGAGCAATGACAGCCACACGTGGGTCACTGTTAAGAATGGATCT GGAGACATGATATTTGAGGGAAACAGTGAGAAGGAGATCCCTGTTCTCAATGAGCTACCCGT CCCCATGGTGGCCCGCTACATCCGCATAAACCCTCAGTCCTGGTTTGATAATGGGAGCATCT GCATGAGAATGGAGATCCTGGGCTGCCCACTGCCAGATCCTAATAATTATTATCACCGCCGG AACGAGATGACCACCACTGATGACCTGGATTTTAAGCACCACAATTATAAGGAAATGCGCCA GTTGATGAAAGTTGTGAATGAAATGTGTCCCAATATCACCAGAATTTACAACATTGGAAAAA GCCACCAGGGCCTGAAGCTGTATGCTGTGGAGATCTCAGATCACCCTGGGGAGCATGAAGTC GGTGAGCCCGAGTTCCACTACATCGCGGGGGCCCACGGCAATGAGGTGCTGGGCCGGGAGCT GCTGCTGCTGGTGCAGTTCGTGTCAGGAGTACTTGGCCCGGAATGCGCGCATCGTCC ACCTGGTGGAGAGACGCGGATTCACGTCCTCCCCTCCAACCCCGATGGCTACGAGAAG GCCTACGAAGGGGGCTCGGAGCTGGGAGCTGGTCCCTGGGACGCTGGACCCACGATGGAAT TGACATCAACAACAACTTTCCTGATTTAAACACGCTGCTCTGGGAGGCAGAGGATCGACAGA ATGTCCCCAGGAAAGTTCCCAATCACTATATTGCAATCCCTGAGTGGTTTCTGTCGGAAAAT GGGCGGCAACCTGCAGGGCGGGGGGGTGGTGGTGGCGTATCCCTACGACCTGGTGCGGTCCC TCCTATGCCTCCACACACCGCCTCATGACAGACGCCCGGAGGAGGGTGTGCCACACGGAGGA CTTCCAGAAGGAGGGCACTGTCAATGGGGCCTCCTGGCACACCGTCGCTGGAAGTCTGA ACGATTTCAGCTACCTTCATACAAACTGCTTCGAACTGTCCATCTACGTGGGCTGTGATAAA TACCCACATGAGAGCCAGCTGCCCGAGGAGTGGGAGAATAACCGGGAATCTCTGATCGTGTT CATGGAGCAGGTTCATCGTGGCATTAAAGGCTTGGTGAGAGATTCACATGGAAAAGGAATCC CAAACGCCATTATCTCCGTAGAAGGCATTAACCATGACATCCGAACAGCCAACGATGGGGAT TACTGGCGCCTCCTGAACCCTGGAGAGTATGTGGTCACAGCAAAGGCCGAAGGTTTCACTGC ATCCACCAAGAACTGTATGGTTGGCTATGACATGGGGGCCACAAGGTGTGACTTCACACTTA GCAAAACCAACATGGCCAGGATCCGAGAGATCATGGAGAAGTTTGGGAAGCAGCCCGTCAGC ${ t CTGCCAGCCAGGCGGCTGAAGCTGCGGGGGGGGGGGAAGAGACGACAGCGTGGG{ t CCTCCTG}}$ GACTCACTCACTGTTTTCCTCTGTAATTCAAGAAGTGCCTGGAAGAGGGGTGCATTGTG AGGCAGGTCCCAAAAGGGAAGGCTGGAGGCTGAGGCTGTTTTCTTTTCTTTGTTCCCATTTA TCCAAATAACTTGGACAGAGCAGCAGAGAAAAGCTGATGGGAGTGAGAGAACTCAGCAAGCC AACCTGGGAATCAGAGAGAGAAGGAGGAGGGGGAGCCTGTCCGTTCAGAGCCTCTGGCTGC

36/340 **FIGURE 35B**

3千/3い **FIGURE 36**

MSRPGTATPALALVLLAVTLAGVGAQGAALEDPDYYGQEIWSREPYYARPEPELETFSPPLP
AGPGEEWERRPQEPRPPKRATKPKKAPKREKSAPEPPPPGKHSNKKVMRTKSSEKAANDDHS
VRVAREDVRESCPPLGLETLKITDFQLHASTVKRYGLGAHRGRLNIQAGINENDFYDGAWCA
GRNDLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSHTWVTVKNGSGDMIF
EGNSEKEIPVLNELPVPMVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTT
TDDLDFKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHPGEHEVGEPEF
HYIAGAHGNEVLGRELLLLLVQFVCQEYLARNARIVHLVEETRIHVLPSLNPDGYEKAYEGG
SELGGWSLGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAA
ETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAYSYAST
HRLMTDARRRVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHES
QLPEEWENNRESLIVFMEQVHRGIKGLVRDSHGKGIPNAIISVEGINHDIRTANDGDYWRLL
NPGEYVVTAKAEGFTASTKNCMVGYDMGATRCDFTLSKTNMARIREIMEKFGKQPVSLPARR
LKLRGRKRRQRG

38 /310 **FIGURE 37**

 $\tt CTAAGAGGACAAG{\color{red} ATG} AGGCCCGGCCTCTCATTTCTCCTAGCCCTTCTGTTCTTCCTTGGCC$ AAGCTGCAGGGGATTTGGGGGATGTGGGACCTCCAATTCCCAGCCCCGGCTTCAGCTCTTTC CCAGGTGTTGACTCCAGCTCCAGCTCCAGCTCCAGGTCGGGCTCCAGCTCCAGCCG CAGCTTAGGCAGCGGAGGTTCTGTGTCCCAGTTGTTTTCCAATTTCACCGGCTCCGTGGATG ACCGTGGGACCTGCCAGTGCTCTGTTTCCCTGCCAGACACCCTTTCCCGTGGACAGAGTG GAGGGAATATGTCCAATTAATTAGTGTGTATGAAAAGAAACTGTTAAACCTAACTGTCCGAA TTGACATCATGGAGAAGGATACCATTTCTTACACTGAACTGGACTTCGAGCTGATCAAGGTA GAAGTGAAGGAGATGGAAAAACTGGTCATACAGCTGAAGGAGAGTTTTGGTGGAAGCTCAGA AATTGTTGACCAGCTGGAGGTGGAGATAAGAAATATGACTCTCTTGGTAGAGAAGCTTGAGA CACTAGACAAAACAATGTCCTTGCCATTCGCCGAGAAATCGTGGCTCTGAAGACCAAGCTG AAAGAGTGTGAGGCCTCTAAAGATCAAAACACCCCTGTCGTCCACCCCTCCCCACTCCAGG ${\tt GAGCTGTGGTGTGTGTGTGAACATCAGCAAACCGTCTGTGGTTCAGCTCAACTGGA}$ ${\tt GGACTGTATTGGGTGGCGCCATTGAATACAGATGGGAGACTGTTGGAGTATTATAGACTGTA}$ CAACACACTGGATGATTTGCTATTGTATAAAATGCTCGAGAGTTGCGGATCACCTATGGCC ${\tt AAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAACATGTACAACACCGGGAAT}$ ATTGCCAGAGTTAACCTGACCACCAACACGATTGCTGTGACTCAAACTCTCCCTAATGCTGC $\tt CTATAATAACCGCTTTTCATATGCTAATGTTGCTTGGCAAGATATTGACTTTGCTGTGGATG$ AGAATGGATTGTGGGTTATTTATTCAACTGAAGCCAGCACTGGTAACATGGTGATTAGTAAA CTCAATGACACCACACTTCAGGTGCTAAACACTTGGTATACCAAGCAGTATAAACCATCTGC TTCTAACGCCTTCATGGTATGTGGGGTTCTGTATGCCACCCGTACTATGAACACCAGAACAG AAGAGATTTTTTACTATTATGACACAAACACAGGGAAAGAGGGGCAAACTAGACATTGTAATG CATAAGATGCAGGAAAAAGTGCAGAGCATTAACTATAACCCTTTTGACCAGAAACTTTATGT $\tt CTATAACGATGGTTACCTTCTGAATTATGATCTTTCTGTCTTGCAGAAGCCCCAG{\red{TAA}GCTG}$ ATATCTGCAGGGGTGTCTAAAAGTGTGTTCATTTTGCAGCAATGTTTAGGTGCATAGTTCTA CCACACTAGAGATCTAGGACATTTGTCTTGATTTGGTGAGTTCTCTTGGGAATCATCTGCCT CTTCAGGCGCATTTTGCAATAAAGTCTGTCTAGGGTGGGATTGTCAGAGGTCTAGGGGCACT GTGGGCCTAGTGAAGCCTACTGTGAGGAGGCTTCACTAGAAGCCTTAAATTAGGAATTAAGG AACTTAAAACTCAGTATGGCGTCTAGGGATTCTTTGTACAGGAAATATTGCCCAATGACTAG CACCTGGAATGATGCTTTGTATGTGGCAGATAAGTAAATTTGGCATGCTTATATATTCTACA TCTGTAAAGTGCTGAGTTTTATGGAGAGAGGCCTTTTTATGCATTAAATTGTACATGGCAAA TAAATCCCAGAAGGATCTGTAGATGAGGCACCTGCTTTTTCTTTTCTCTCATTGTCCACCTT AACCAGACTTACTAACCAATTCCACCCCCCCCCCCCCTTCTACTGCCTACTTTAAAAAA TGGACTTTTATTTACATGACTCTAAGACTATAAGAAAATCTGATGGCAGTGACAAAGTGCTA GCATTTATTGTTATCTAATAAAGACCTTGGAGCATATGTGCAACTTATGAGTGTATCAGTTG TTGCATGTAATTTTTGCCTTTGTTTAAGCCTGGAACTTGTAAGAAAATGAAAATTTAATTTT TTTTTCTAGGACGAGCTATAGAAAAGCTATTGAGAGTATCTAGTTAATCAGTGCAGTAGTTG GAAACCTTGCTGGTGTATGTGATGTGCTTCTGTGCTTTTGAATGACTTTATCATCTAGTCTT TGTCTATTTTTCCTTTGATGTTCAAGTCCTAGTCTATAGGATTGGCAGTTTAAATGCTTTAC

39 /310 **FIGURE 38**

MRPGLSFLLALLFFLGQAAGDLGDVGPPIPSPGFSSFPGVDSSSSFSSSSRSGSSSSRSLGS
GGSVSQLFSNFTGSVDDRGTCQCSVSLPDTTFPVDRVERLEFTAHVLSQKFEKELSKVREYV
QLISVYEKKLLNLTVRIDIMEKDTISYTELDFELIKVEVKEMEKLVIQLKESFGGSSEIVDQ
LEVEIRNMTLLVEKLETLDKNNVLAIRREIVALKTKLKECEASKDQNTPVVHPPPTPGSCGH
GGVVNISKPSVVQLNWRGFSYLYGAWGRDYSPQHPNKGLYWVAPLNTDGRLLEYYRLYNTLD
DLLLYINARELRITYGQGSGTAVYNNNMYVNMYNTGNIARVNLTTNTIAVTQTLPNAAYNNR
FSYANVAWQDIDFAVDENGLWVIYSTEASTGNMVISKLNDTTLQVLNTWYTKQYKPSASNAF
MVCGVLYATRTMNTRTEEIFYYYDTNTGKEGKLDIVMHKMQEKVQSINYNPFDQKLYVYNDG
YLLNYDLSVLQKPQ

40/310 **FIGURE 39**

GCTCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAACACCCCTGTCGTCCAC
CCTCCTCCCACTCCAGGGAGCTGTGGTCATGGTGGTGTGAACATCAGCAAACCGTCTGT
GGTTCAGCTCAACTGGAGAGGGTTTTCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTC
CCCAGCATCCAAACAAAGGNATGTATTGGGNGGCGCCATTGAATACAGATGGGAGACTGTTG
GAGTATTATAGACTGTACAACCCACTGGATGATTTGCTATTGTATATAAATGCTCGAGAGTT
GCGGATCACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAACA

 ${\tt CCGCTGCTCTTGTGACGTTGTGGAG} \underline{{\tt ATC}} {\tt GGGAGCGTCCTGGGGGCTGTGCTCCATGGCGAGCT}$ $\overline{\text{GGATACCATGTTTGTGTGGAAGTGCCCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAAACC}}$ TGTAATGTTGATACCAGGAATGGAAGAACAACTGAATAAGATTCCTGGATTTTGTGAGAATG AGAAAGGTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTT GGTTTGGCTATGTTCTATCTTCTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGA TCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTA TTATTGGGGCATTCTTCATTCCAGAAGGAACTTTTACAACTGTGTGGTTTTATGTAGGCATG GAATGAATCGTGGGTTGAAAAAATGGAAGAAGGGAACTCGAGATGTTGGTATGCAGCCTTGT TATCAGCTACAGCTCTGAATTATCTGCTGTCTTTAGTTGCTATCGTCCTGTTCTTTGTCTAC TACACTCATCCAGCCAGTTGTTCAGAAAACAAGGCGTTCATCAGTGTCAACATGCTCCTCTG CGTTGGTGCTTCTGTAATGTCTATACTGCCAAAAATCCAAGAATCACAACCAAGATCTGGTT TGTTACAGTCTTCAGTAATTACAGTCTACACAATGTATTTGACATGGTCAGCTATGACCAAT GAACCAGAAACAAATTGCAACCCAAGTCTACTAAGCATAATTGGCTACAATACAACAAGCAC TGTCCCAAAGGAAGGCAGTCAGTCCAGTGGTGGCATGCTCAAGGAATTATAGGACTAATTC TCTTTTTGTTGTGTGTATTTTATTCCAGCATCCGTACTTCAAACAATAGTCAGGTTAATAAA CTGACTCTAACAAGTGATGAATCTACATTAATAGAAGATGGTGGAGCTAGAAGTGATGGATC ACTGGAGGATGGGGACGATGTTCACCGAGCTGTAGATAATGAAAGGGATGGTGTCACTTACA GTTATTCCTTCTTCACTTCATGCTTTTCCTGGCTTCACTTTATATCATGATGACCCTTACC AACTGGTCCAGGTATGAACCCTCTCGTGAGATGAAAAGTCAGTGGACAGCTGTCTGGGTGAA ${\tt AATCTCTTCCAGTTGGATTGGCATCGTGCTGTTTTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGTTCCCAGTTGGACACTCGTGGCACCACTTGTTCCCAGTTGTTCCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTGTTCCAGTTCA$ ${ t TTACAAATCGTGATTTTGAC} { t TGA} { t GTGAGACTTCTAGCATGAAAGTCCCACTTTGATTATTGC}$ ${\tt TTATTTGAAAACAGTATTCC}\overline{{\tt CAA}}{\tt CTTTTGTAAAGTTGTGTATGTTTTTGCTTCCCATGTAAC}$ TTCTCCAGTGTTCTGGCATGAATTAGATTTTACTGCTTGTCATTTTGTTATTTTCTTACCAA GTGCATTGATATGTGAAGTAGAATGAATTGCAGAGGAAAGTTTTATGAATATGGTGATGAGT TAGTAAAAGTGGCCATTATTGGGCTTATTCTCTGCTCTATAGTTGTGAAATGAAGAGTAAAA GCAAATGTATGGCTGCCTTTTGAAATATTTGATGTGTTGCCTGGCAGGATACTGCAAAGAAC ATGGTTTATTTAAAATTTATAAACAAGTCACTTAAATGCCAGTTGTCTGAAAAATCTTATA AGGTTTTACCCTTGATACGGAATTTACACAGGTAGGGAGTGTTTAGTGGACAATAGTGTAGGTTA TGGATGGAGGTGTCGGTACTAAATTGAATAACGAGTAAATAATCTTACTTGGGTAGAGATGG CCTTTGCCAACAAGTGAACTGTTTTGGTTGTTTTAAACTCATGAAGTATGGGTTCAGTGGA AATGTTTGGAACTCTGAAGGATTTAGACAAGGTTTTGAAAAGGATAATCATGGGTTAGAAGG AAGTGTTTTGAAAGTCACTTTGAAAGTTAGTTTTTGGGCCCAGCACGGTAGCTCACCCTTGGT AATCCCAGCACTTTGGGAGCTTAAGTGGGTAGATTACTTGAGCCCAGGAATTCAGACCAGCT TGGCACATGGTGAACCTGTTCTATAAAAATAATCTGGCTTTGAGCATATGCCTGTGGTCCAG CACTGAGAGGCTAGTGAAGATTGCTGAGCCCAGAGCCAAAGGTTGCAGTGAGCAAGTCACGT CAAAATTTTGACAGGAAGGAAGTAACTGCAAAACCACTAGGCTTTAGTAGGTACTTATATA AAATCTAGTCCAGTTCTCTCATTTAAAAAAATGAAGACACTGAAATACAGACTTAAATAGCT CAGATAGCTAATTAGGAAATTTCAAGTTGGCCAATAATAGCATTCTCTCTGACATTTAAAAA GTGGATTGCTGGTGTCCAGCATGACCCATAAACAGGTCAGAAGAATGATGGAATGTTTTAGA ATAAACTCCTGCTTATAGTATACTACACAGTTCAAAAGATGTTTAAAATGCTTTTGTATTTA CTGCCATGTAATTGAAATATATAGATTATTGTAACCTTTCAACCTGAAAATCAAGCAGTATG AGAGTTTAGTTATTTGTATGTCTCACTAGTGTCTAATGAAGCTTTTAAAATCTACAATTTCT TCTTTAAAAATATTTATTAATGTGAATGGAATATAACAATTCAGCTTAATTCCCCCAACCTTA AATTCAGAGAAAAAAAAAAAAA

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FIGURE 41

MGSVLGLCSMASWIPCLCGSAPCLLCRCCPSGNNSTVTRLIYALFLLVGVCVACVMLIPGME
EQLNKIPGFCENEKGVVPCNILVGYKAVYRLCFGLAMFYLLLSLLMIKVKSSSDPRAAVHNG
FWFFKFAAAIAIIIGAFFIPEGTFTTVWFYVGMAGAFCFILIQLVLLIDFAHSWNESWVEKM
EEGNSRCWYAALLSATALNYLLSLVAIVLFFVYYTHPASCSENKAFISVNMLLCVGASVMSI
LPKIQESQPRSGLLQSSVITVYTMYLTWSAMTNEPETNCNPSLLSIIGYNTTSTVPKEGQSV
QWWHAQGIIGLILFLLCVFYSSIRTSNNSQVNKLTLTSDESTLIEDGGARSDGSLEDGDDVH
RAVDNERDGVTYSYSFFHFMLFLASLYIMMTLTNWSRYEPSREMKSQWTAVWVKISSSWIGI
VLYVWTLVAPLVLTNRDFD

FIGURE 42

GCGAGAAAGAAGCTGTCTCCATCTTGTCTGTATCCCGCTGCTTCTTGNGACGTTGTGGAGAT
GGGGAGCGTCCCTGGGGCTGCTCCATGGCGAGCTGGATACCATGTTTGTGTGGAAGTGCC
CCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAAACAANTCCACTGTAACTAGATTGATCTA
TGCACTTTTCTTGCTTGTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAG
AACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATT
TTGGTTGGCTATAAAGCTGTATATCGTTTGTGTTTTGGTTTGGCTATGTTCTTCTT
CTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCACAATGGAT
TTTGGTTCTTTAAATTTTGCTGCAGCAATTGCAATTATTATTGGGGC

цц/3¬0 **FIGURE 43**

GTTATTGTGAACTTTGTGGAGATGGGAGGTCNTGGGGCTGTTTCCATGGCGAGCTGGATAC
CANGTTTGTGTGGAAGTGCCCCGTGTTTGNTATGCCGATGCTGTCCTAGTGGAAACAANTCC
ACTGTAATTAGATTGATNTATGCACTTTTNTTGCTTGTTGGAGTANGTGTAGCTTGTGTAAT
GTTGATACCAGGAATGGAAGAACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAG
GTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATNGTTTGTGCTTTGGTTTG
GCTANGTTCTATNTTCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAG
AGCTGCAGTGCACAATGGATTTTGGTTTTTAAATTTGCTGCAGCAATTGCAATTATTATTG
GGGC

FIGURE 44

FIGURE 45

FIGURE 46A

GGCCTCTCCAATGGCAAATGTGTGTGGCTGGAGGCGAGCCGAGGCTTTCGGCAAAGGCAGT CGAGTGTTTGCAGACCGGGGCGAGTCCTGTGAAAGCAGATAAAAGAAAACATTTATTAACGT GTCATTACGAGGGGAGCGCCCGGGGGCTGTCGCACTCCCCGCGGAACATTTGGCTCCCT CCAGCTCCGAGAGAGAGAAGAAGAGCGGAAAAGAGGCAGATTCACGTCGTTTCCAGCCA AGTGGACCTGATGGCCCTCCTGAATTTATCACGATATTTGATTTATTAGCGATGCCCC $\tt CTGGTTTGTGTTACGCACACACACGTGCACACAAGGCTCTGGCTCGCTTCCCTCGT$ GAGTGTGTCGAATCTGCGAGTGAAGAGGGGACGAGGGGAAAAGAAACAAAGCCACAGACGCAAC GCCTCGTGCTGCTGCTGTCCGCAACTGTGTTCTCCCTGCTGGGTGGAAGCTCGGCCTTC $\tt CTGTCGCACCGCCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCCAACAT$ CATCCTGGTGCTGACGACGACCAGGATGTGGAGCTGGGTTCCATGCAGGTGATGAACAAGA CCCGGCGCATCATGGAGCAGGGCGGGGCGCACTTCATCAACGCCTTCGTGACCACACCCATG TGCTGCCCCTCACGCTCCTCCATCCTCACTGGCAAGTACGTCCACAACCACAACACCTACAC CAACAATGAGAACTGCTCCTCGCCCTCCTGGCAGGCACAGCACGAGAGCCGCACCTTTGCCG GGCTCCTACGTGCCACCCGGCTGGAAGGAGTGGGTCGGACTCCTTAAAAACTCCCGCTTTTA TAACTACACGCTGTGTCGGAACGGGGTGAAAGAGAAGCACGGCTCCGACTACTCCAAGGATT ACCTCACAGACCTCATCACCAATGACAGCGTGAGCTTCTTCCGCACGTCCAAGAAGATGTAC CCGCACAGGCCAGTCCTCATGGTCATCAGCCATGCAGCCCCCCACGGCCCTGAGGATTCAGC CCCACAATATTCACGCCTCTTCCCAAACGCATCTCAGCACATCACGCCGAGCTACAACTACG CGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGGCCCATGAAGCCCATCCACATG GAATTCACCAACATGCTCCAGCGGAAGCGCTTGCAGACCCTCATGTCGGTGGACGACTCCAT GGAGACGATTTACAACATGCTGGTTGAGACGGGCGAGCTGGACAACACGTACATCGTATACA CCGCCGACCACGGTTACCACATCGGCCAGTTTGGCCTGGTGAAAGGGAAATCCATGCCATAT ${\tt GAGTTTGACATCAGGGTCCCGTTCTACGTGAGGGGCCCCAACGTGGAAGCCGGCTGTCTGAA}$ TCCCCACATCGTCCTCAACATTGACCTGGCCCCCACCATCCTGGACATTGCAGGCCTGGACA TACCTGCGGATATGGACGGGAAATCCATCCTCAAGCTGCTGGACACGGAGCGGCCGGTGAAT CGGTTTCACTTGAAAAAGAAGATGAGGGTCTGGCGGGACTCCTTCTTGGTGGAGAGAGGCAA GCTGCTACACAAGAGAGACAATGACAAGGTGGACGCCCAGGAGGAGAACTTTCTGCCCAAGT ACCAGCGTGTGAAGGACCTGTGTCAGCGTGCTGAGTACCAGACGGCGTGTGAGCAGCTGGGA ${\tt CAGAAGTGGCAGTGTGGAGGACGCCACGGGGAAGCTGAAGCTGCATAAGTGCAAGGGCCCC}$ CATGCGGCTGGGCGGCAGCAGCCCTCTCCAACCTCGTGCCCAAGTACTACGGGCAGGGCA GCGAGGCCTGCACCTGTGACAGCGGGGACTACAAGCTCAGCCTGGCCGGACGCCGGAAAAAA CTCTTCAAGAAGAAGTACAAGGCCAGCTATGTCCGCAGTCGCTCCATCCGCTCAGTGGCCAT CGAGGTGGACGGCAGGGTGTACCACGTAGGCCTGGGTGATGCCGCCCAGCCCCGAAACCTCA ${\tt CCAAGCGGCACTGGCCAGGGGCCCCTGAGGACCAAGATGACAAGGATGGTGGGGACTTCAGT}$ GGCACTGGAGGCCTTCCCGACTACTCAGCCGCCAACCCCATTAAAGTGACACATCGGTGCTA CATCCTAGAGAACGACACAGTCCAGTGTGACCTGGACCTGTACAAGTCCCTGCAGGCCTGGA AAGACCACAAGCTGCACATCGACCACGAGATTGAAACCCTGCAGAACAAAATTAAGAACCTG AGGGAAGTCCGAGGTCACCTGAAGAAAAAGCGGCCAGAAGAATGTGACTGTCACAAAATCAG CTACCACACCAGCACAAAGGCCGCCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTCAGGA AGGGCCTGCAAGAAGGACAAGGTGTGGCTGTTGCGGGAGCAGAAGCGCAAGAAGAAACTC $\tt CGCAAGCTGCTCAAGCGCCTGCAGAACAACGACACGTGCAGCCTCACGTGCTT$ ${\tt CACCCACGACAACCAGCACTGGCAGACGGCGCCTTTCTGGACACTGGGGCCTTTCTGTGCCT}$ GCACCAGCGCCAACAATAACACGTACTGGTGCATGAGGACCATCAATGAGACTCACAATTTC

FIGURE 46B

CTCTTCTGTGAATTTGCAACTGGCTTCCTAGAGTACTTTGATCTCAACACAGACCCCTACCA GCTGATGAATGCAGTGAACACACTGGACAGGGATGTCCTCAACCAGCTACACGTACAGCTCA TGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAACCCCCGGACTCGAAACATGGACCTG GATGGAGGAAGCTATGAGCAATACAGGCAGTTTCAGCGTCGAAAGTGGCCAGAAATGAAGAG ${\tt ACCTTCTTCCAAATCACTGGGACAACTGTGGGAAGGCTGGGAAGGT} {\color{blue}{\textbf{TAA}}} {\color{blue}{\textbf{GAAACAACAGAGG}}}$ TGGACCTCCAAAAACATAGAGGCATCACCTGACTGCACAGGCAATGAAAAACCATGTGGGTG AACATGACAGATTCTGGAGGATAACCAGCAGGAGCAGAGATAACTTCAGGAAGTCCATTTTT GCCCCTGCTTTTGCTTTGGATTATACCTCACCAGCTGCACAAAATGCATTTTTTCGTATCAA GATTTCCTTGGAAATTTCTCCCAAGGGCGAAAGTCATTGGAATTTTTAAATCATAGGGGAAA AGCAGTCCTGTTCTAAATCCTCTTATTCTTTTGGTTTGTCACAAAGAAGGAACTAAGAAGCA ${\tt GGACAGAGGCAACGTGGAGAGGCTGAAAACAGTGCAGAGACGTTTGACAATGAGTCAGTAGC}$ ACAAAAGAGATGACATTTACCTAGCACTATAAACCCTGGTTGCCTCTGAAGAAACTGCCTTC ATTGTATATATGTGACTATTTACATGTAATCAACATGGGAACTTTTAGGGGAACCTAATAAG AAATCCCAATTTTCAGGAGTGGTGGTCAATAAACGCTCTGTGGCCAGTGTAAAAGAAAAA

FIGURE 47

MGPPSLVLCLLSATVFSLLGGSSAFLSHHRLKGRFQRDRRNIRPNIILVLTDDQDVELGSMQ
VMNKTRRIMEQGGAHFINAFVTTPMCCPSRSSILTGKYVHNHNTYTNNENCSSPSWQAQHES
RTFAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSD
YSKDYLTDLITNDSVSFFRTSKKMYPHRPVLMVISHAAPHGPEDSAPQYSRLFPNASQHITP
SYNYAPNPDKHWIMRYTGPMKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNT
YIVYTADHGYHIGQFGLVKGKSMPYEFDIRVPFYVRGPNVEAGCLNPHIVLNIDLAPTILDI
AGLDIPADMDGKSILKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVDAQEEN
FLPKYQRVKDLCQRAEYQTACEQLGQKWQCVEDATGKLKLHKCKGPMRLGGSRALSNLVPKY
YGQGSEACTCDSGDYKLSLAGRRKKLFKKKYKASYVRSRSIRSVAIEVDGRVYHVGLGDAAQ
PRNLTKRHWPGAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQCDLDLYKS
LQAWKDHKLHIDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGRLKHRGSSL
HPFRKGLQEKDKVWLLREQKRKKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLG
PFCACTSANNNTYWCMRTINETHNFLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQL
HVQLMELRSCKGYKQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

FIGURE 48

AACAAAGTTCAGTGACTGAGAGGGCTGAGCGGAGGCTGCTGAAGGGGGAGAAAGGAGTGAGGA ${\tt GCTGCTGGGCAGAGAGGGACTGTCCGGCTCCCAG} \underline{{\tt ATG}} {\tt CTGGGGCAGAGGCACAGCCC}$ TCGTGGGATGATCACAGGTGCTGCTGTGGCGGTCCTGCTGCTGCTGCTGCTGCCACC TGCCTTTTCCACGGACGGCAGGACTGTGACGTGGAGAGGAACCGTACAGCTGCAGGGGGAAA ${\tt CCGAGTCCGCCGGGCCCAGCCTTGGCCCTTCCGGCGGGGCCCACCTGGGAATCTTTCACC}$ $\texttt{CGCTCGC} \underline{\textbf{TGA}} \texttt{GGCTGCTGTCGCCGGTGCCTGTCGACAGCAGCTGCCCTGCCCTTCCCATCTG}$ TTCCCAGGACAAGTGGACCCCATGTTTCCATGTGGAAGGATGCATCTCTGGGGTGAACGAGG GGAACAATAGACTGGGGCTTGCTCCAGCTGCATTTGCATGGCATGCCCCAGTGTACTATGGC AGCAGAGAATGGAGGAACACTGGGTCTGCAGTGCTGAAGGGTTTGGGGAGTGGAGAGCAAGG GTGCTCTTTCGGGGCTGGACAGCCCGTCTTGTGACAGTGACTCCCAGTGAGCCCCAGAAATG ${\tt ATCAGGCTGCAGGCCTCTGGCGGGCAGGGCACTGGGAGAGGCCCTGAGAATGTCCTTTT}$ GGTTTGGAGAAGGCAGTGAGGCTGCACAGTCAATTCATCGGTGCCTTAGTCCAAGAAAAT

 ${\tt MLGLLGSTALVGWITGAAVAVLLLLLLLATCLFHGRQDCDVERNRTAAGGNRVRRAQPWPFR} \\ RRGHLGIFHHHRHPGHVSHVPNVGLHHHHHPRHTPHHLHHHHHPHRHHPRHAR} \\$

5シ/3ハロ **FIGURE 50**

GGCGGCTGCTGAGCTGCCTTGAGGTGCAGTGTTGGGGATCCAGAGCCATGTCGGACCTGCTA CTACTGGGCCTGATTGGGGGCCTGACTCTTTACTGCTGCTGACGCTGCTGGCCTTTGCCGG GTACTCAGGGCTACTGGCTGGGTGGAAGTGAGTGCTGGGTCACCCCCCATCCGCAACGTCA CTGTGGCCTACAAGTTCCACATGGGGCTCTATGGTGAGACTGGGCGGCTTTTCACTGAGAGC TGCAGCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCC CCCTGATAAGTGCCGATGTGCCGTGGGCAGCATCCTGAGTGAAGGTGAGGAATCGCCCTCCC CTGAGCTCATCGACCTCTACCAGAAATTTGGCTTCAAGGTGTTCTCCTTCCCGGCACCCAGC TGTCCATCCTGCCTTGGACACCTACATCAAGGAGCGGAAGCTGTGTGCCTATCCTCGGCTGG AGATCTACCAGGAAGACCAGATCCATTTCATGTGCCCACTGGCACGGCAGGGAGACTTCTAT GTGCCTGAGATGAAGGAGACAGAGTGGAAATGGCGGGGGCTTGTGGAGGCCATTGACACCCA GGTGGATGGCACAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAGTGAGCC CTGGCAGCCGGGAGACTTCAGCTGCCACACTGTCACCTGGGGCGAGCCGTGGCTGGGAT GACGGTGACACCCGCAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTCTTTTGA GGAGCTGGACTTGGAGGGCCCGAGGGCCCTTAGGGGAGTCACGGCTGGACCCTGGGACTGAGC ${\tt CCCTGGGGACTACCAAGTGGCTCTGGGAGCCCACTGCCCCTGAGAAGGGCAAGGAG{\color{blue}{\textbf{TAA}}} CCC}$ ATGGCCTGCACCCTCCTGCAGTGCAGTTGCTGAGGAACTGAGCAGACTCTCCAGCAGACTCT CCAGCCCTCTTCCTCCTCTGGGGGGGGGGGGGTTCCTGAGGGACCTGACTTCCCCTGC TCCAGGCCTCTTGCTAAGCCTTCTCCTCACTGCCCTTTAGGCTCCCAGGGCCAGAGGAGCCA GGGACTATTTTCTGCACCAGCCCCCAGGGCTGCCGCCCCTGTTGTGTCTTTTTTCAGACTC ACAGTGGAGCTTCCAGGACCCAGAATAAAGCCAATGATTTACTTGTTTCACCTGGAAAAAA AAAAAAAA

FIGURE 51

MSDLLLLGLIGGLTLLLLLTLLAFAGYSGLLAGVEVSAGSPPIRNVTVAYKFHMGLYGETGR LFTESCSISPKLRSIAVYYDNPHMVPPDKCRCAVGSILSEGEESPSPELIDLYQKFGFKVFS FPAPSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHFMCPLAR QGDFYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAATLSPGAS SRGWDDGDTRSEHSYSESGASGSSFEELDLEGEGPLGESRLDPGTEPLGTTKWLWEPTAPEKGKE

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54/310 FIGURE 52

MTLRPSLLPLHLLLLLLSAAVCRAEAGLETESPVRTLQVETLVEPPEPCAEPAAFGDTLHI
HYTGSLVDGRIIDTSLTRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRAIIPSHLAYGKRGF
PPSVPADAVVQYDVELIALIRANYWLKLVKGILPLVGMAMVPALLGLIGYHLYRKANRPKVS
KKKLKEEKRNKSKKK

CCGAAAGTCCCGTCCGGACCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCC
GAGCCCGCTGCTTTTGGAGACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACG
TATTATTGACACCTCCCTGACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGA
TTCCAGGTCTGGAGCAGAGTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATT
CCTTCTCACTTGGCCTATGGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGT
GCAGTATGACGTGGAGCTGATTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGG
GCATTTTGCCTCTGGTAGGGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCAC
CTATACAGAAAAGGCCAATAGACCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAA
CAAGAGCAAAAAGAAATAATAAATAAATAAATTTTTAAAAAACTTTAAAA

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FIGURE 56

CTGCTGCATCCGGGTGTCTGGAGGCTGTGGCCGTTTTGTTTTCTTGGCTAAAATCGGGGGAG TGAGGCGGCCGGCGCGCGACACCGGGCTCCGGAACCACTGCACGACGGGGCTGGACTG ACCTGAAAAAATGTCTGGATTTCTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGG GAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGAT TATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGATTTCAACCACTCATACCATGCCT GTGGTGTTATAGCAACCATAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGA GGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGG TTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTG CTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATCTTT ${\tt TTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGACTTATGGCAG} {\tt TGA} {\tt ACACATCTGAT}$ TTGTAATGCCATTTTCTAAACTTATTTCTGAGTGTAGTCTCAGCTTAAAGTTGTGTAATACT AAAATCACGAGAACACCTAAACAACCAAAAAATCTATTGTGGTATGCACTTGATTAACTT ATAAAATGTTAGAGGAAACTTTCACATGAATAATTTTTTGTCAAATTTTATCATGGTATAATT TGTAAAAATAAAAGAAATTACAAAAGAAATTATGGATTTGTCAATGTAAGTATTTGTCATA TCTGAGGTCCAAAACCACAATGAAAGTGCTCTGAAGATTTAATGTGTTTATTCAAATGTGGT CTCTTCTGTGTCAAATGTTAAATGAAATATAAACATTTTTTAGTTTTTAAAATATTCCGTGG TCAAAATTCTTCCTCACTATAATTGGTATTTACTTTTACCAAAAATTCTGTGAACATGTAAT GTAACTGGCTTTTGAGGGTCTCCCAAGGGGTGAGTGGACGTGTTGGAAGAGAGAAGCACCAT GGTCCAGCCACCAGGCTCCCTGTGTCCCTTCCATGGGAAGGTCTTCCGCTGTGCCTCTCATT CCAAGGCAGGAAGATGTGACTCAGCCATGACACGTGGTTCTGGTGGGATGCACAGTCACTC CACATCCACCACTG

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53/310 FIGURE 57

MSGFLEGLRCSECIDWGEKRNTIASIAAGVLFFTGWWIIIDAAVIYPTMKDFNHSYHACGVI ATIAFLMINAVSNGQVRGDSYSEGCLGQTGARIWLFVGFMLAFGSLIASMWILFGGYVAKEK DIVYPGIAVFFQNAFIFFGGLVFKFGRTEDLWQ

TGGACGGACCTGAAAAAATGTTTGGATTTNTAGAGGGNTTGAGATGTTCAGAATGCATGAC
TGGGGGAAAAGCGCAAATACTATTGCTTCCATTGCTGCTGGTGTANTATTTTTTACAGGCTG
GTGGATTATCATAGATGCAGNTGTTATTTATCCCACCATGAAAGATTTCAACCANTCATACC
ATGCCTGTGGTGTTATAGCAACCATAGCCTTCNTAATGATTAATGCAGTATCGAATGGACAA
GTCCGAGGTGATAGTTACAGTGAAGGTTGTTTGGGTCAAACAGGTGCTCGCATTTGGCTTTT
CGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTT
ATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGNTGTATTTTTCCAGAATGCCTTC
ATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGANTTATGGCAGTG

GGACACCGGGTTCCGGACCAATGCANGACGGGGTGGANTGACCTGAAAAAAATGTTTGGATT
TTTAGAGGGCTTGAGATGNTCAGAATGCATTGACTGGGGGAAAAGCGCAATANTATTGCTTT
CCATTGCTGCTGGTGTACTATTTTTTACAGGGTGGTGGATTATCATAGATGCAGCTGTTATT
TATCCCACCATGAAAGATTTNAACCACTCATACCATGCCTGTGGTGTTATAGCAACCATAGC
CTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTT
GTTTGGGTCAAACAGGTGNTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATTT
CTGATTGNATTCTATGCGGATTCTTCTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTAT
ACCCTGGAATTNCTNTATTTTTCCAGAATGCC

FIGURE 61

TAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATANTATTGCTTCC
ATTGNTGNTGGTGTANTATTTTTTTACAGGCTGGTGGATTATNATAGATGCAGCTGTTATTT
ATCCCACCATGAAAGATTTNAACCANTCATACCATGCCTGTGGTGTTATAGCAACCATAGCC
TTCCTAATGATTAATGCAGTATNGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTG
TTTGGGTCAAACAGGTGNTNGCATTTGGCTTTTNGTTGGTTTCATGTTGGCCTTTGGATCTN
TGATTGCATTTATGTGGATTNTTTTTTGGAGGTTATGTTGCTAAAGNAAAAGACATAGTATAC
CCTGT

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FIGURE 62

FIGURE 63

TCTGCAAAGTTTACTTGGGACTATTCTCTGGCAGCTCCCCGAATCCTTTCTCCGAAGATGTC AAACGGCCCCCAGCGCCCCTGGTAACTGACAAGGAGGCCAGGAAGAAGGTTCTCAAACAAGC TTTTTCAGCCAACCAAGTGCCGGAGAAGCTGGATGTGGTGATTTGGCAGTGGCTTTGGGG GCCTGGCTGCAGCTGCAATTCTAGCTAAAGCTGGCAAGCGAGTCCTGGTGCTGGAACAACAT ACCAAGGCAGGGGGCTGCTGTCATACCTTTGGAAAGAATGGCCTTGAATTTGACACAGGAAT CCATTACATTGGGCGTATGGAAGAGGGCAGCATTGGCCGTTTTATCTTGGACCAGATCACTG AAGGGCAGCTGGACTGGGCTCCCCTGTCCTCTCTTTTGACATCATGGTACTGGAAGGGCCC AATGGCCGAAAGGAGTACCCCATGTACAGTGGAGAGAAAGCCTACATTCAGGGCCTCAAGGA GAAGTTTCCACAGGAGGAAGCTATCATTGACAAGTATATAAAGCTGGTTAAGGTGGTATCCA GTGGAGCCCCTCATGCCATCCTGTTGAAATTCCTCCCATTGCCCGTGGTTCAGCTCCTCGAC AGGTGTGGGCTGACTCGTTTCTCTCCATTCCTTCAAGCATCCACCCAGAGCCTGGCTGA GGTCCTGCAGCAGCTGGGGGCCTCCTCTGAGCTCCAGGCAGTACTCAGCTACATCTTCCCCA CTTACGGTGTCACCCCCAACCACAGTGCCTTTTCCATGCACGCCCTGCTGGTCAACCACTAC ATGAAAGGAGGCTTTTATCCCCGAGGGGGTTCCAGTGAAATTGCCTTCCACACCATCCCTGT GATTCAGCGGGCTGGGGGCGCTGTCCTCACAAAGGCCACTGTGCAGAGTGTGTTGCTGGACT CAÇCTGGGAAAGCCTGTGGTGTCAGTGTGAAGAAGGGGCCATGAGCTGGTGAACATCTATTGC CCCATCGTGGTCTCCAACGCAGGACTGTTCAACACCTATGAACACCTACTGCCGGGGAACGC CCGCTGCCTGCCAGGTGTGAAGCAGCAACTGGGGACGGTGCGGCCCGGCTTAGGCATGACCT CTGTTTTCATCTGCCTGCGAGGCACCAAGGAAGACCTGCATCTGCCGTCCACCAACTACTAT GTTTACTATGACACGGACATGGACCAGGCGATGGAGCGCTACGTCTCCATGCCCAGGGAAGA GGCTGCGGAACACATCCCTCTTCTTCTTCTTCGCTTTCCCATCAGCCAAAGATCCGACCTGGG AGGACCGATTCCCAGGCCGGTCCACCATGATCATGCTCATACCCACTGCCTACGAGTGGTTT GAGGAGTGGCAGGCGGAGCTGAAGGGAAAGCGGGGCAGTGACTATGAGACCTTCAAAAACTC CTTTGTGGAAGCCTCTATGTCAGTGGTCCTGAAACTGTTCCCACAGCTGGAGGGGAAGGTGG AGAGTGTGACTGCAGGATCCCCACTCACCAACCAGTTCTATCTGGCTGCTCCCCGAGGTGCC TGCTACGGGGCTGACCATGACCTGGGCCGCCTGCACCCTTGTGTGATGGCCTCCTTGAGGGC CCAGAGCCCCATCCCCAACCTCTATCTGACAGGCCAGGATATCTTCACCTGTGGACTGGTCG GGGCCCTGCAAGGTGCCCTGCTGCAGCAGCGCCATCCTGAAGCGGAACTTGTACTCAGAC ${\tt CTTAAGAATCTTGATTCTAGGATCCGGGCACAGAAGAAAAGAAT} \underline{{\tt TAG}} {\tt TTCCATCAGGGAGG}$ AGTCAGAGGAATTTGCCCAATGGCTGGGGCATCTCCCTTGACTTACCCATAATGTCTTTCTG TTTAAATCACAATTCCGAATCTGGGGCAATGGAATCACTGCTTCCAGCTGGGGCAGGTGAGA TCTTTACGCCTTTTATAACATGCCATCCCTACTAATAGGATATTGACTTGGATAGCTTGATG TCTCATGACGAGCGCGCTCTGCATCCCTCACCCATGCCTCAACTCAGTGATCAAAGCGA ATATTCCATCTGTGGATAGAACCCCTGGCAGTGTTGTCAGCTCAACCTGGTGGGTTCAGTTC TGTCCTGAGGCTTCTGCTCTCATTCATTTAGTGCTACGCTGCACAGTTCTACACTGTCAAGG GAAAAGGGAGACTAATGAGGCTTAACTCAAAACCTGGGCGTGGTTTTGGTTGCCATTCCATA GGTTTGGAGAGCTCTAGATCTCTTTTGTGCTGGGTTCAGTGGCTCTTCAGGGGACAGGAAAT GCCTGTGTCTGGCCAGTGTGGTTCTGGAGCTTTGGGGTAACAGCAGGATCCATCAGTTAGTA CTTATCCACCAAATACACAGGGAAGGGTGATGCAGGGAAGGGTGACATCAGGAGTCAGGGCA TGGACTGGTAAGATGAATACTTTGCTGGGCTGAAGCAGGCTGCAGGGCATTCCAGCCAAGGG CACAGCAGGGGACAGTGCAGGGAGGTGTGGGGTAAGGGAAGGTCACATCAGAAAAGGGA AAGCCACGGAATGTGTGTGAAGCCCAGAAATGGCATTTGCAGTTAATTAGCACATGTGAGGG TTAGACAGGTAGGTGAATGCAAGCTCAAGGTTTGGAAAAATGACTTTTCAGTTATGTCTTTG GTATCAGACATACGAAAGGTCTCTTTGTAGTTCGTGTTAATGTAACATTAATAAATTTATTG ATTCCATTGCTTTAAAAAAAAAAAAAAAAA

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66/310 FIGURE 64

MWLPLVLLLAVLLLAVLCKVYLGLFSGSSPNPFSEDVKRPPAPLVTDKEARKKVLKQAFSAN QVPEKLDVVVIGSGFGGLAAAAILAKAGKRVLVLEQHTKAGGCCHTFGKNGLEFDTGIHYIG RMEEGSIGRFILDQITEGQLDWAPLSSPFDIMVLEGPNGRKEYPMYSGEKAYIQGLKEKFPQ EEAIIDKYIKLVKVVSSGAPHAILLKFLPLPVVQLLDRCGLLTRFSPFLQASTQSLAEVLQQ LGASSELQAVLSYIFPTYGVTPNHSAFSMHALLVNHYMKGGFYPRGGSSEIAFHTIPVIQRA GGAVLTKATVQSVLLDSAGKACGVSVKKGHELVNIYCPIVVSNAGLFNTYEHLLPGNARCLP GVKQQLGTVRPGLGMTSVFICLRGTKEDLHLPSTNYYVYYDTDMDQAMERYVSMPREEAAEH IPLLFFAFPSAKDPTWEDRFPGRSTMIMLIPTAYEWFEEWQAELKGKRGSDYETFKNSFVEA SMSVVLKLFPQLEGKVESVTAGSPLTNQFYLAAPRGACYGADHDLGRLHPCVMASLRAQSPI PNLYLTGQDIFTCGLVGALQGALLCSSAILKRNLYSDLKNLDSRIRAQKKKN

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64/310 FIGURE 65

GCAGCGGCGAGGCGGCGGTGGTGGCTGAGTCCGTGGTGGCAGAGGCGAAGGCGACAGCTCTA GGGGTTGGCACCGGCCCCGAGAGGAGGATGCGGGTCCGGATAGGGCTGACGCTGCTGCTGTG TGCGGTGCTGCTGAGCTTGGCCTCGGCGTCCTCGGATGAAGAAGGCAGCCAGGATGAATCCT GTAGTTGCTGGTCAAATATTTCTTGATTCAGAAGAATCTGAATTAGAATCCTCTATTCAAGA AGAGGAAGACAGCCTCAAGAGCCAAGAGGGGGGAAAGTGTCACAGAAGATATCAGCTTTCTAG ACCGCCATTGAAGGCACAGCACATGGGGAGCCCTGCCACTTCCCTTTTCTTTTCCTAGATAA GGAGTATGATGAATGTACATCAGATGGGAGGGAAGATGGCAGACTGTGGTGTGCTACAACCT ATGACTACAAAGCAGATGAAAAGTGGGGCTTTTTGTGAAACTGAAGAAGAGGCTGCTAAGAGA CGGCAGATGCAGGAAGCAGAAATGATGTATCAAACTGGAATGAAAATCCTTAATGGAAGCAA CCAAAGCCCTGGAGAGAGTGTCATATGCTCTTTTATTTGGTGATTACTTGCCACAGAATATC CAGGCAGCGAGAGAGATGTTTGAGAAGCTGACTGAGGAAGGCTCTCCCAAGGGACAGACTGC TCTTGGCTTTCTGTATGCCTCTGGACTTGGTGTTAATTCAAGTCAGGCAAAGGCTCTTGTAT ATTATACATTTGGAGCTCTTGGGGGCAATCTAATAGCCCACATGGTTTTGGTAAGTAGACTT $\underline{\textbf{TAG}} \textbf{TGGAAGGCTAATAATATTAACATCAGAAGAATTTGTGGTTTATAGCGGCCACAACTTTT}$ ATTCTTGTTAATGGATATAACACATGGAATCTACATGTAAATGAAAGTTGGTGGAGTCCACA ATTTTTCTTTAAAATGATTAGTTTGGCTGATTGCCCCTAAAAAGAGAGATCTGATAAATGGC TCTTTTTAAATTTTCTCTGAGTTGGAATTGTCAGAATCATTTTTTACATTAGATTATCATAA TTTTAAAAATTTTTCTTTAGTTTTTCAAAATTTTTGTAAATGGTGGCTATAGAAAAACAACAT GAAATATTATACAATATTTTGCAACAATGCCCTAAGAATTGTTAAAATTCATGGAGTTATTT GTGCAGAATGACTCCAGAGAGCTCTACTTTCTGTTTTTTACTTTTCATGATTGGCTGTCTTC CCATTTATTCTGGTCATTTATTGCTAGTGACACTGTGCCTGCTTCCAGTAGTCTCATTTTCC CTATTTTGCTAATTTGTTACTTTTCTTTGCTAATTTGGAAGATTAACTCATTTTTAATAAA ΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑ

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68/310 FIGURE 66

MRVRIGLTLLLCAVLLSLASASSDEEGSQDESLDSKTTLTSDESVKDHTTAGRVVAGQIFLD SEESELESSIQEEEDSLKSQEGESVTEDISFLESPNPENKDYEEPKKVRKPALTAIEGTAHG EPCHFPFLFLDKEYDECTSDGREDGRLWCATTYDYKADEKWGFCETEEEAAKRRQMQEAEMM YQTGMKILNGSNKKSQKREAYRYLQKAASMNHTKALERVSYALLFGDYLPQNIQAAREMFEK LTEEGSPKGQTALGFLYASGLGVNSSQAKALVYYTFGALGGNLIAHMVLVSRL

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FIGURE 67

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FIGURE 68

MACRCLSFLLMGTFLSVSQTVLAQLDALLVFPGQVAQLSCTLSPQHVTIRDYGVSWYQQRAG SAPRYLLYYRSEEDHHRPADIPDRFSAAKDEAHNACVLTISPVQPEDDADYYCSVGYGFSP

CGCTGCTGCTGGGGGCCTTCCCACCGGCCGCCGCCCGAGGCCCCCCAAAGATGGCGGAC AAGGTGGTCCCACGGCAGGTGGCCCGGCTGGGCCGCACTGTGCGCCCAGTGGA GGGGGACCCGCCGCCGCTGACCATGTGGACCAAGGATGGCCGCACCATCCACAGCGGCTGGA GCCGCTTCCGCGTGCTGCCGCAGGGGCTGAAGGTGAAGCAGGTGGAGCGGGAGGATGCCGGC GTGTACGTGTGCAAGGCCACCAACGGCTTCGGCAGCCTGAGCGTCAACTACACCCTCGTCGT GCTGGATGACATTAGCCCAGGGAAGGAGAGCCTGGGGGCCCGACAGCTCCTCTGGGGGTCAAG AGGACCCCGCCAGCCAGCAGTGGGCACGACCGCGCTTCACACAGCCCTCCAAGATGAGGCGC CGGGTGATCGCACGGCCCGTGGGTAGCTCCGTGCGGCTCAAGTGCGTGGCCAGCGGGCACCC TCGGCCCGACATCACGTGGATGAAGGACGACCAGGCCTTGACGCGCCCAGAGGCCGCTGAGC ACCTGCCGCGTGTCGAACCGCGCGCGCCCATCAACGCCACCTACAAGGTGGATGTGATCCA GCGGACCCGTTCCAAGCCCGTGCTCACAGGCACGCACCCCGTGAACACGACGGTGGACTTCG GGGGGACCACGTCCTTCCAGTGCAAGGTGCGCAGCGACGTGAAGCCGGTGATCCAGTGGCTG AAGCGCGTGGAGTACGGCGCCGAGGGCCCACAACTCCACCATCGATGTGGGCGGCCAGAA GTTTGTGGTGCCCACGGGTGACGTGTGGTCGCGGCCCGACGGCTCCTACCTCAATAAGC TGCTCATCACCCGTGCCCGCCAGGACGATGCGGGCATGTACATCTGCCTTGGCGCCAACACC ATGGGCTACAGCTTCCGCAGCGCCTTCCTCACCGTGCTGCCAGACCCAAAACCGCCAGGGCC ${\tt ACCTGTGGCCTCGTCGTCGTCGCCACTAGCCTGCCGTGGCCCGTGGTCATCGGCATCCCAG}$ ${\tt CCGGCGCTGTCTTCATCCTGGGCACCCTGCTCCTGTGGCTTTGCCAGGCCCAGAAGAAGCCG}$ TGCACCCCGCGCCTGCCCTGCCTGGCCACCGCCGGGGACGGCCCGCGACCG CAGCGGAGACAAGGACCTTCCCTCGTTGGCCGCCCTCAGCGCTGGCCCTGGTGTGGGGCTGT GTGAGGAGCATGGGTCTCCGGCAGCCCCCAGCACTTACTGGGCCCAGGCCCAGTTGCTGGC ${ t ACACTCACACGTGGAGGGCAAGGTCCACCAGCACTATCAGTGC} { t TAG} { t ACACTCACTATCAGTGC} { t ACACTCACTAGTGC} { t ACACTCACTCACTAGTGC} { t ACACTCACTAGTGC} { t ACACTCACTAGTGC} { t ACACTCACTAGTGC} { t ACACTCACTAGTGC} { t ACACTCACTCACTAGTGC} { t ACACTCACTAGTGC} { t ACACTCACTAGTGC} { t ACACTCACTCACTAGTGC} { t ACACTCACTAGTGC} { t ACACTCACTACTAGTGC} { t ACACTCACTACTAGTGC} { t ACACTCACTACTAGTGC} { t ACACTCACTACTAGTGC} { t ACACTCAC$ ATCTGCAGTGGGCACGGGGGGGCCAGACAGGCAGACTGGGAGGATGGAGGACGGAGCT GCAGACGAAGGCAGGGGACCCATGGCGAGGAGGAATGGCCAGCACCCCAGGCAGTCTGTGTG TGAGGCATAGCCCCTGGACACACACACACACACACACACTACCTGGATGCATGTATGCAC ACACATGCGCGCACACGTGCTCCCTGAAGGCACACGTACGCACACGCACATGCACAGATATG CCGCCTGGGCACACAGATAAGCTGCCCAAATGCACGCACACGCACAGAGACATGCCAGAACA TACAAGGACATGCTGCCTGAACATACACACGCACACCCATGCGCAGATGTGCTGCCTGGACA CACACACACACGGATATGCTGTCTGGACGCACACGTGCAGATATGGTATCCGGACACA ATATTGCCTGGACACACACACACACGCGTGCACAGATATGCTGTCTGGACACGCACAC ACATGCAGATATGCTGCCTGGACACACACTTCCAGACACACGTGCACAGGCGCAGATATGCT TGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATATGCTGTCCGGATACACACG GCAGATATGCTGCCTGGACACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGA TATTGCCTGGACACACACATGTGCACAGATATGCTGTCTGGACATGCACACGTGCAGATA TGCTGTCCGGATACACACGCACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGA CACACATGCACACAGGTGCAGATATGCTGCCTGGACACACGCAGACTGACGTGCTTTTGG GAGGGTGTGCCGTGAAGCCTGCAGTACGTGTGCCGTGAGGCTCATAGTTGATGAGGGACTTT CCCTGCTCCACCGTCACTCCCCCAACTCTGCCCGCCTCTGTCCCCGCCTCAGTCCCCGCCTC CATCCCCGCCTCTGTCCCCTGGCCTTGGCGGCTATTTTTGCCACCTGCCTTGGGTGCCCAGG AGTCCCCTACTGCTGTGGGCTGGGGTTGGGGGCACAGCCCCAAGCCTGAGAGGCTGGAG CCCATGGCTAGTGGCTCATCCCCAGTGCATTCTCCCCCTGACACAGAGAAGGGGCCTTGGTA TTTATATTTAAGAAATGAAGATAATATTAATAATGATGGAAGGAAGACTGGGTTGCAGGGAC TGTGGTCTCTCCTGGGGCCCGGGACCCGCCTGGTCTTTCAGCCATGCTGATGACCACACCCC GTCCAGGCCAGACACCACCCCCACCCCACTGTCGTGGTGGCCCCAGATCTCTGTAATTTTA

MTPSPLLLLLPPLLLGAFPPAAAARGPPKMADKVVPRQVARLGRTVRLQCPVEGDPPPLTM
WTKDGRTIHSGWSRFRVLPQGLKVKQVEREDAGVYVCKATNGFGSLSVNYTLVVLDDISPGK
ESLGPDSSSGGQEDPASQQWARPRFTQPSKMRRRVIARPVGSSVRLKCVASGHPRPDITWMK
DDQALTRPEAAEPRKKKWTLSLKNLRPEDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVL
TGTHPVNTTVDFGGTTSFQCKVRSDVKPVIQWLKRVEYGAEGRHNSTIDVGGQKFVVLPTGD
VWSRPDGSYLNKLLITRARQDDAGMYICLGANTMGYSFRSAFLTVLPDPKPPGPPVASSSSA
TSLPWPVVIGIPAGAVFILGTLLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSGDKDLPS
LAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLYPKLYTDIHTHTHTHSHTHSHVEGKV
HQHIHYQC

FIGURE 71A

CCCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAAACTTCCCAGGGGACCG CATTCCAGAGTCAGTGACTCTGTGAAGCACCCACATCTACCTCTTGCCACGTTCCCACGGGC $\tt TTGGGGGAAAG\underline{ATG}\tt GTGGGGACCAAGGCCTGGGTGTTCTCCTTGCTGGTCCTGGAAGTCACA$ TCTGTGTTGGGGAGACAGACGATGCTCACCCAGTCAGTAAGAAGAGTCCAGCCTGGGAAGAA GAACCCCAGCATCTTTGCCAAGCCTGCCGACACCCTGGAGAGCCCCTGGTGAGTGGACAACAT GGTTCAACATCGACTACCCAGGCGGGAAGGGCGACTATGAGCGGCTGGACGCCATTCGCTTC ACCTGCGGGCAGCACTGGCCAGGTGGTCCATGGTAGTCCCCGTGAGGGTTTCTGGTGCCTCA ACAGGGAGCAGCCTGGCCAGAACTGCTCTAATTACACCGTACGCTTCCTCTGCCCACCA GGATCCCTGCGCCGAGACACAGAGCGCATCTGGAGCCCATGGTCTCCCTGGAGCAAGTGCTC AGCTGCCTGTGGTCAGACTGGGGTCCAGACTCGCACACGCATTTGCTTGGCAGAGATGGTGT ${\tt CGCTGTGCAGTGAGGCCAGCGAAGAGGGTCAGCACTGCATGGGCCAGGACTGTACAGCCTGT}$ GACCTGACCTGCCCAATGGGCCAGGTGAATGCTGACTGTGATGCCTGCATGTGCCAGGACTT CATGCTTCATGGGGCTGTCTCCCTTCCCGGAGGTGCCCCAGCCTCAGGGGCTGCTATCTACC GGCTTGTGCCCTGATGGCAAAAGCATCCTGAAGATCACAAAGGTCAAGTTTGCCCCCATTGT ACTCACAATGCCCAAGACTAGCCTGAAGGCAGCCACCATCAAGGCAGAGTTTGTGAGGGCAG ${\tt AGACTCCATACATGGTGATGAACCCTGAGACAAAAGCACGGAGAGCTGGGCAGAGCGTGTCT}$ CTGTGCTGTAAGGCCACAGGGAAGCCCAGGCCAGACAAGTATTTTTGGTATCATAATGACAC ATTGCTGGATCCTTCCCTCTACAAGCATGAGAGCAAGCTGGTGCTGAGGAAACTGCAGCAGC ACCAGGCTGGGGAGTACTTTTGCAAGGCCCAGAGTGATGCTGGGGCTGTGAAGTCCAAGGTT GCCCAGCTGATTGTCACAGCATCTGATGAGACTCCTTGCAACCCAGTTCCTGAGAGCTATCT TATCCGGCTGCCCCATGATTGCTTTCAGAATGCCACCAACTCCTTCTACTATGACGTGGGAC GCTGCCCTGTTAAGACTTGTGCAGGGCAGCAGGATAATGGGATCAGGTGCCGTGATGCTGTG CAGAACTGCTGTGGCATCTCCAAGACAGAGGAAAGGGAGATCCAGTGCAGTGGCTACACGCT ACCCACCAAGGTGGCCAAGGAGTGCAGCTGCCAGCGGTGTACGGAAACTCGGAGCATCGTGC GGGGCCGTGTCAGTGCTGACAATGGGGAGCCCATGCGCTTTGGCCATGTGTACATGGGG AACAGCCGTGTAAGCATGACTGGCTACAAGGGCACTTTCACCCTCCATGTCCCCCAGGACAC TGAGAGGCTGGTGCTCACATTTGTGGACAGGCTGCAGAAGTTTGTCAACACCACCAAAGTGC TACCTTTCAACAAGAAGGGGAGTGCCGTGTTCCATGAAATCAAGATGCTTCGTCGGAAAGAG CCCCATGGCTGAACTGGAGATTCCATCCAGGAGTTTCTACAGGCAGAATGGGGAGCCCTACA TAGGAAAAGTGAAGGCCAGTGTGACCTTCCTGGATCCCCGGAATATTTCCACAGCCACAGCT ... GCCCAGACTGACCTGAACTTCATCAATGACGAAGGAGACACTTTCCCCCCTTCGGACGTATGG CATGTTCTCTGTGGACTTCAGAGATGAGGTCACCTCAGAGCCACTTAATGCTGGCAAAGTGA AGGTCCACCTTGACTCGACCCAGGTCAAGATGCCAGAGCACATATCCACAGTGAAACTCTGG TCACTCAATCCAGACACAGGGCTGTGGGAGGAGGAAGGTGATTTCAAATTTGAAAATCAAAG TCTTTAACCTGGATGTTCCTGAAAGCAGGCGGTGCTTTGTTAAGGTGAGGGCCTACCGGAGT GAGAGGTTCTTGCCTAGTGAGCAGATCCAGGGGGTTGTGATCTCCGTGATTAACCTGGAGCC TAGAACTGGCTTCTTGTCCAACCCTAGGGCCTGGGGCCGCTTTGACAGTGTCATCACAGGCC CCAACGGGGCCTGTGTGCCTTCTGTGATGACCAGTCCCCTGATGCCTACTCTGCCTAT GTCTTGGCAAGCCTGGCTGGGAGGAACTGCAAGCAGTGGAGTCTTCTCCTAAATTCAACCC AGGATCCACGGGTTAAAAAGACAGCTTTCCAGATTAGCATGGCCAAGCCAAGGCCCAACTCA GCTGAGGAGGAGCAATGGGCCCATCTATGCCTTTGAGAACCTCCGGGCATGTGAAGAGGCACC ACCCAGTGCAGCCCACTTCCGGTTCTACCAGATTGAGGGGGGATCGATATGACTACAACACAG TCCCCTTCAACGAAGATGACCCTATGAGCTGGACTGAAGACTATCTGGCATGGTGGCCAAAG CCGATGGAATTCAGGGCCTGCTATATCAAGGTGAAGATTGTGGGGCCCACTGGAAGTGAATGT GCGATCCCGCAACATGGGGGGCACTCATCGGCGGACAGTGGGGAAGCTGTATGGAATCCGAG ATGTGAGGAGCACTCGGGACAGGGACCAGCCCAATGTCTCAGCTGCCTGTCTGGAGTTCAAG TGCAGTGGGATGCTCTATGATCAGGACCGTGTGGACCGCACCCTGGTGAAGGTCATCCCCCA GGGCAGCTGCCGTCGAGCCAGTGTGAACCCCATGCTGCATGAGTACCTGGTCAACCACTTGC CACTTGCAGTCAACAACGACACCAGTGAGTACACCATGCTGGCACCCTTGGACCCACTGGGC CACAACTATGGCATCTACACTGTCACTGACCAGGACCCTCGCACGGCCAAGGAGATCGCGCT CGGCCGGTGCTTTGATGGCACATCCGATGGCTCCTCCAGAATCATGAAGAGCAATGTGGGAG TAGCCCTCACCTTCAACTGTGTAGAGAGGCAAGTAGGCCGCCAGAGTGCCTTCCAGTACCTC CAAAGCACCCCAGCCCAGTCCCCTGCTGCAGGCACTGTCCAAGGAAGAGTGCCCTCGAGGAG GCAGCAGCGAGCGAGCAGGGTGGCCAGCGCCAGGGTGGAGTGGCCTCTCTGAGATTTC

F14/310 FIGURE 71B

MVGTKAWVFSFLVLEVTSVLGRQTMLTQSVRRVQPGKKNPSIFAKPADTLESPGEWTTWFNI DYPGGKGDYERLDAIRFYYGDRVCARPLRLEARTTDWTPAGSTGQVVHGSPREGFWCLNREQ RPGQNCSNYTVRFLCPPGSLRRDTERIWSPWSPWSKCSAACGQTGVQTRTRICLAEMVSLCS ${\tt EASEEGQHCMGQDCTACDLTCPMGQVNADCDACMCQDFMLHGAVSLPGGAPASGAAIYLLTK}$ TPKLLTQTDSDGRFRIPGLCPDGKSILKITKVKFAPIVLTMPKTSLKAATIKAEFVRAETPY MVMNPETKARRAGQSVSLCCKATGKPRPDKYFWYHNDTLLDPSLYKHESKLVLRKLQQHQAG ${\tt EYFCKAQSDAGAVKSKVAQLIVTASDETPCNPVPESYLIRLPHDCFQNATNSFYYDVGRCPV}$ $\tt KTCAGQQDNGIRCRDAVQNCCGISKTEEREIQCSGYTLPTKVAKECSCQRCTETRSIVRGRV$ ${\tt SAADNGEPMRFGHVYMGNSRVSMTGYKGTFTLHVPQDTERLVLTFVDRLQKFVNTTKVLPFN}$ KKGSAVFHEIKMLRRKEPITLEAMETNIIPLGEVVGEDPMAELEIPSRSFYRQNGEPYIGKV KASVTFLDPRNISTATAAQTDLNFINDEGDTFPLRTYGMFSVDFRDEVTSEPLNAGKVKVHL DSTQVKMPEHISTVKLWSLNPDTGLWEEEGDFKFENQRRNKREDRTFLVGNLEIRERRLFNL DVPESRRCFVKVRAYRSERFLPSEQIQGVVISVINLEPRTGFLSNPRAWGRFDSVITGPNGA CVPAFCDDQSPDAYSAYVLASLAGEELQAVESSPKFNPNAIGVPQPYLNKLNYRRTDHEDPR VKKTAFQISMAKPRPNSAEESNGPIYAFENLRACEEAPPSAAHFRFYQIEGDRYDYNTVPFN EDDPMSWTEDYLAWWPKPMEFRACYIKVKIVGPLEVNVRSRNMGGTHRRTVGKLYGIRDVRS TRDRDQPNVSAACLEFKCSGMLYDQDRVDRTLVKVIPQGSCRRASVNPMLHEYLVNHLPLAV ${\tt NNDTSEYTMLAPLDPLGHNYGIYTVTDQDPRTAKEIALGRCFDGTSDGSSRIMKSNVGVALT}$ ${\tt FNCVERQVGRQSAFQYLQSTPAQSPAAGTVQGRVPSRRQQRASRGGQRQGGVVASLRFPRVA}$ OOPLIN

CTGCAAGTTGTTAACGCCTAACACACAAGTATGTTAGGCTTCCACCAAAGTCCTCAATATAC CTGAATACGCACAATATCTTAACTCTTCATATTTGGTTTTGGGATCTGCTTTGAGGTCCCAT ${\tt TTACAAAGAATTTAGAG} \underline{{\tt ATG}} {\tt TATTTGTCAAGATCCCTGTCGATTCATGCCCTTTGGGTTACG}$ GTGTCCTCAGTGATGCAGCCCTACCCTTTGGTTTGGGGACATTATGATTTGTGTAAGACTCA GATTTACACGGAAGGAAGGTTTGGGATTACATGGCCTGCCAGCCGGAATCCACGGACA TGACAAAATATCTGAAAGTGAAACTCGATCCTCCGGATATTACCTGTGGAGACCCTCCTGAG ACGTTCTGTGCAATGGGCAATCCCTACATGTGCAATAATGAGTGTGATGCGAGTACCCCTGA ${\tt AGTCTGCCACTTGGAAGGAGTATCCCAAGCCTCTCCAGGTTAACATCACTCTGTCTTGGAGC}$ AAAACCATTGAGCTAACAGACAACATAGTTATTACCTTTGAATCTGGGCGTCCAGACCAAAT GATCCTGGAGAAGTCTCTCGATTATGGACGAACATGGCAGCCCTATCAGTATTATGCCACAG ACTGCTTAGATGCTTTTCACATGGATCCTAAATCCGTGAAGGATTTATCACAGCATACGGTC TTAGAAATCATTTGCACAGAAGAGTACTCAACAGGGTATACAACAAATAGCAAAATAATCCA $\tt CTTTGAAATCAAAGACAGGTTCGCGCTTTTTGCTGGACCTCGCCTACGCAATATGGCTTCCC$ TCTACGGACAGCTGGATACAACCAAGAAACTCAGAGATTTCTTTACAGTCACAGACCTGAGG ATAAGGCTGTTAAGACCAGCCGTTGGGGAAATATTTGTAGATGAGCTACACTTGGCACGCTA CTTTTACGCGATCTCAGACATAAAGGTGCGAGGAAGGTGCAAGTGTAATCTCCATGCCACTG TATGTGTGTATGACAACAGCAAATTGACATGCGAATGTGAGCACAACACTACAGGTCCAGAC TGTGGGAAATGCAAGAAGAATTATCAGGGCCGACCTTGGAGTCCAGGCTCCTATCTCCCCAT CCCCAAAGGCACTGCAAATACCTGTATCCCCAGTATTTCCAGTATTGGTACGAATGTCTGCG ACAACGAGCTCCTGCACTGCCAGAACGGAGGGACGTGCCACAACAACGTGCGCTGCCTGTGC CCGGCCGCATACACGGGCATCCTCTGCGAGAAGCTGCGGTGCGAGGAGGCTGGCAGCTGCGG CTCCGACTCTGGCCAGGGCGCGCCCCGCACGCACCCCAGCGCTGCTGCTGACCACGC ${ t TGCTGGGAACCGCCAGCCCCTGGTGTTC}{ t TAG}{ t GTGTCACCTCCAGCCACACCGGACGGGCCT}$ AGACACCCCCACTCAGACAGTGTACAAACTAAGAAGGCCTAACTGAACTAAGCCATATTTAT CACCCGTGGACAGCACATCCGAGTCAAGACTGTTAATTTCTGACTCCAGAGGAGTTGGCAGC TGTTGATATTATCACTGCAAATCACATTGCCAGCTGCAGAGCATATTGTGGATTGGAAAGGC TTCTTTGCTGTCAGGTGCATTGTGGGCATAAGGAAATCTGTTACAAGCTGCCATATTGGCCT GCTTCCGTCCCTGAATCCCTTCCAACCTGTGCTTTAGTGAACGTTGCTCTGTAACCCTCGTT GGTTGAAAGATTTCTTTGTCTGATGTTAGTGATGCACATGTGTAACAGCCCCCCTCTAAAAGC ATTTTTCTTGAACTACTGTAATATGTAGATTTTTTGTATTATTGCCAATTTGTGTTACCAGA ${\tt CAATCTGTTAATGTATCTAATTCGAATCAGCAAAGACTGACATTTTATTTTGTCCTCTTTCG}$ GAATATCAGTTTACATATAACAAGTGTAATAAGATTCCACCAAAGGACATTCTAAATGTT TTCTTGTTGCTTTAACACTGGAAGATTTAAAGAATAAAAACTCCTGCATAAACGATTTCAGG ${\tt ACTGATTTCTGTGTGGACTGAGTACATTCAGCTGACGAATTTAGTTCCCAGGAAGATGGATT}$ GATGTTCACTAGCTTGGACAACTTCTGCAAAATATGAGACTATTTCCACTTGGGAAAAATTA СААСАССАААААААААААААААААА

MYLSRSLSIHALWVTVSSVMQPYPLVWGHYDLCKTQIYTEEGKVWDYMACQPESTDMTKYLK
VKLDPPDITCGDPPETFCAMGNPYMCNNECDASTPELAHPPELMFDFEGRHPSTFWQSATWK
EYPKPLQVNITLSWSKTIELTDNIVITFESGRPDQMILEKSLDYGRTWQPYQYYATDCLDAF
HMDPKSVKDLSQHTVLEIICTEEYSTGYTTNSKIIHFEIKDRFALFAGPRLRNMASLYGQLD
TTKKLRDFFTVTDLRIRLLRPAVGEIFVDELHLARYFYAISDIKVRGRCKCNLHATVCVYDN
SKLTCECEHNTTGPDCGKCKKNYQGRPWSPGSYLPIPKGTANTCIPSISSIGTNVCDNELLH
CQNGGTCHNNVRCLCPAAYTGILCEKLRCEEAGSCGSDSGQGAPPHGTPALLLLTTLLGTAS
PLVF

WO 99/63088 PCT/US99/12252

FIGURE 75

CCCACGCGTCCGGGTGACCTGGGCCGAGCCCTCCCGGTCGGCTAAGATTGCTGAGGAGGCGG ${\tt CGGGTAGCTGGCAGGCGCGACTTCCGAAGGCCGCCGTCCGGGCGAGGTGTCCTCATGACTT}$ $\tt CTCTTGTGGACC \underline{ATG} \tt TCCGTGATCTTTTTTGCCTGCGTGGTACGGGTAAGGGATGGACTGCC$ CCTCTCAGCCTCTACTGATTTTTACCACACCCAAGATTTTTTGGAATGGAGGAGACGGCTCA ${\tt AGAGTTTAGCCTTGCGACTGGCCCAGTATCCAGGTCGAGGTTCTGCAGAAGGTTGTGACTTT}$ AGTATACATTTTTCTTCTTCGGGGACGTGGCCTGCATGGCTATCTGCTCCTGCCAGTGTCC AGCAGCCATGGCCTTCTGCTTCCTGGAGACCCTGTGGTGGGAATTCACAGCTTCCTATGACA $\tt CTACCTGCATTGGCCTAGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTCAG$ AAAGTGAAGTGCCATTTTAACTATGTAAGTTCCTCTCAGATGGAGTGCAGCTTGGAAAAAAT TCAGGAGGAGCTCAAGTTGCAGCCTCCAGCGGTTCTCACTCTGGAGGACACAGATGTGGCAA ATGGGGTGATGAATGGTCACACACCGATGCACTTGGAGCCTGCTCCTAATTTCCGAATGGAA CCAGTGACAGCCCTGGGTATCCTCTCCCTCATTCTCAACATCATGTGTGCCCTGAATCT CATTCGAGGAGTTCACCTTGCAGAACATTCTTTACAGGATCCAAGGAGCTGGTTCTGCTGGT ${\tt TGGACCAAACCTCG}{\tt TGA}{\tt GCCAGCCACCCCTGACCCAAATGAGGAGAGCTCTGATTCTCCCAT}$ CCGGGAGCAGTGATGTCAAACTTCTGCTGCTGGGGAAATCTCATCAGCAGGGAGCCTGTGGA AAAGGGCATGTCAGTGAAATCTGGGAATGGCTGGATTCGGAAACATCTGCCCATGTGTATTG ATGGCAGAGCTGTTGCCCACAAGCGCCTTTTATTTAGGGTAAAATTAACAAATCCATTCTAT TCCTCTGACCCATGCTTAGTACATATGACCTTTAACCCTTACATTTATATGATTCTGGGGTT GCTTCAGAAGTGTTATTTCATGAATCATTCATATGATTTGATCCCCCAGGATTCTATTTTGT TTAATGGGCTTTTCTACTAAAAGCATAAAATACTGAGGCTGATTTAGTCAGGGCAAAACCAT ${\tt TTACTTTACATATTCGTTTTCAATACTTGCTGTTCATGTTACACAAGCTTCTTACGGTTTTC}$ TTGTAACAATAATATTTTGAGTAAATAATGGGTACATTTTAACAAACTCAGTAGTACAACC TAAACTTGTATAAAAGTGTGTAAAAATGTATAGCCATTTATATCCTATGTATAAATTAAATG **AAAAG**

FIGURE 76

MSVIFFACVVRVRDGLPLSASTDFYHTQDFLEWRRRLKSLALRLAQYPGRGSAEGCDFSIHF SSFGDVACMAICSCQCPAAMAFCFLETLWWEFTASYDTTCIGLASRPYAFLEFDSIIQKVKW HFNYVSSSQMECSLEKIQEELKLQPPAVLTLEDTDVANGVMNGHTPMHLEPAPNFRMEPVTA LGILSLILNIMCAALNLIRGVHLAEHSLQDPRSWFCWLDQTS

 $\label{totalcar} TGCTTCCTGGAGACCCTGTGGTGGGAATTCACAGCTTCNTATGACACTACCTGCATTGGCNT\\ AGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTCAGAAAGTGAAGTGGCATT\\ TTAACTATGTAAGTTCCTNTCAGATGGAGTGCAGCTTGGAAAAAATTCAGGAGGAGCTCAAG\\ TTGCAGCCTCCAGCGGTTCTCANTATGGAGGACACAGATGTGGCAAATGGGGT$

CTCAGCGGCGCTTCCTCGTAGCGAGCCTAGTGGCGGGTGTTTGCATTGAAACGTGAGCGCGA CCCGACCTTAAAGAGTGGGGAGCAAAGGGAGGACAGAGCCCTTTAAAACGAGGCGGGTGGTG CCTGCCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTT TCTGTCGCAGGCTGCGAGGAAAGGCCCCTAGGCTGGGTCTGGGTGCTTGGCGGCGGCGGCTT ${\tt CCTCCCGGTCCTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGT\underline{A}}$ $\underline{\textbf{TG}} \texttt{GAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGC}$ GAGTGTATTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGAC CCGCTTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGA TTGCGCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGCTCCTGCCC TTCTCCATCATCAGCAATGAGGTGCTGCTCTCCCTGCCTCGGAACTACTACATCCAGTGGCT CAACGGCTCCCTCATCCATGGCCTCTGGAACCTTGTTTTTCTCTTCCCCAACCTGTCCCTCA TCTTCCTCATGCCCTTTGCATATTTCTTCACTGAGTCTGAGGGCTTTGCTGGCTCCAGAAAG GGTGTCCTGGGCCGGGTCTATGAGACAGTGGTGATGTTGATGCTCCTCACTCTGCTGGTGCT ${\tt AGGTATGGTGGGGTGGCATCAGCCATTGTGGACAAGAACAAGGCCAACAGAGAGTCACTCT}$ $\tt CTGCTCCTGGTGTACTCCACTGGGTCTCGCCCGCATGTTCTCCGTCACTGGGAAGCTGCT$ AGTCAAGCCCCGGCTGCTGGAAGACCTGGAGGAGCAGCTGTACTGCTCAGCCTTTGAGGAGG TTCAGCCTGGCAACGGAACCTGGGCTACCCCCTGGCTATGCTGTGCTGCTGGTGCTGACGG GCCTGTCTGTGCTCATTGTGGCCATCCACATCCTGGAGCTGCTCATCGATGAGGCTGCCATG CCCCGAGGCATGCAGGTACCTCCTTAGGCCAGGTCTCCTTCTCCAAGCTGGGCTCCTTTGG TGCCGTCATTCAGGTTGTACTCATCTTTTACCTAATGGTGTCCTCAGTTGTGGGCTTCTATA GCTCTCCACTCTTCCGGAGCCTGCGGCCCAGATGGCACGACACTGCCATGACGCAGATAATT ${\tt GGGAACTGTGTCTCTGGTCCTAAGCTCAGCACTTCCTGTCTTCTCTGAACCCTGGG}$ ACTGCAGCTGTGCGGGCAGAGCTGATCCGGGCCTTTGGGCTGGACAGACTGCCGCTGCCCGT $\tt CTCCGGTTTCCCCCAGGCATCTAGGAAGACCCAGCACCAG\underline{TGA}CCTCCAGCTGGGGGTGGGA$ AGGAAAAACTGGACACTGCCATCTGCTGCCTAGGCCTGGAGGGAAGCCCAAGGCTACTTGG ACCTCAGGACCTGGAATCTGAGAGGGTGGGTGGCAGAGGGGAGCAGAGCCATCTGCACTATT GCATAATCTGAGCCAGAGTTTGGGACCAGGACCTCCTGCTTTTCCATACTTAACTGTGGCCT CAGCATGGGGTAGGGCTGGGTGACTGGGTCTAGCCCCTGATCCCAAATCTGTTTACACATCA ATCTGCCTCACTGCTGTTCTGGGCCATCCCCATAGCCATGTTTACATGATTTGATGTGCAAT ${\tt CTTGCCTCTGGCCCAGCAGAGCCTAAGCACTGTGCTATCCTGGAGGGGCTTTGGACCACCTG}$ AAAAA

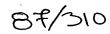
MEAPDYEVLSVREQLFHERIRECIISTLLFATLYILCHIFLTRFKKPAEFTTVDDEDATVNK
IALELCTFTLAIALGAVLLLPFSIISNEVLLSLPRNYYIQWLNGSLIHGLWNLVFLFPNLSL
IFLMPFAYFFTESEGFAGSRKGVLGRVYETVVMLMLLTLLVLGMVWVASAIVDKNKANRESL
YDFWEYYLPYLYSCISFLGVLLLLVCTPLGLARMFSVTGKLLVKPRLLEDLEEQLYCSAFEE
AALTRRICNPTSCWLPLDMELLHRQVLALQTQRVLLEKRRKASAWQRNLGYPLAMLCLLVLT
GLSVLIVAIHILELLIDEAAMPRGMQGTSLGQVSFSKLGSFGAVIQVVLIFYLMVSSVVGFY
SSPLFRSLRPRWHDTAMTQIIGNCVCLLVLSSALPVFSRTLGLTRFDLLGDFGRFNWLGNFY
IVFLYNAAFAGLTTLCLVKTFTAAVRAELIRAFGLDRLPLPVSGFPQASRKTQHQ

FIGURE 80

GGCTGCCGAGGGAAGGCCCCTTGGGTTGGTTTGCTTGGCTGCGGCGGCGGTTTCNTCCCC
GCTCGTCCTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGAAGC
ACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGTGTA
TTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGACCCGCTTC
AAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCG



 ${\tt MLLWVILLVLAPVSGQFARTPRPIIFLQPPWTTVFQGERVTLTCKGFRFYSPQKTKWYHRYL}$ ${\tt GKEILRETPDNILEVQESGEYRCQAQGSPLSSPVHLDFSSEMGFPHAAQANVELLGSSDLLT}$



 ${\tt CAGAAGAGGGGGCTAGCTGTCTCTGCGGACCAGGGAGACCCCCGCGCCCCCCGGTGT}$ ${\tt GAGTGTGTGGAACAGGACCCGGGACAGAGGGAACC} \underline{{\tt ATG}} {\tt GCTCCGCAGAACCTGAGCACCTTTT}$ GCCTGTTGCTGCTATACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTG GGGGTGCCTCGAAGTGCCTCTATAAAGGATATTAAAAAGGCCTATAGGAAACTAGCCCTGCA GCTTCATCCCGACCGGAACCCTGATGATCCACAAGCCCAGGAGAAATTCCAGGATCTGGGTG $\tt CTGCTTATGAGGTTCTGTCAGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA$ ${\tt GGATTAAAAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTCACACTTCTTTGGGGATTT}$ TGGTTTCATGTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATA ${\tt TTATTGTAGAAGTCACTTTGGAAGAAGTATATGCAGGAAATTTTGTGGAAGTAGTT}$ AGAAACAAACCTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTCGGCAAGAGAT GCGGACCACCCAGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAAT GCCCTAATGTCAAACTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTG ${\tt AGAGACGGCATGGAGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG}$ AGATTTACGGTTCCGAATCAAAGTTGTCAAGCACCCAATATTTGAAAGGAGAGGAGATGATT ${\tt TGTACACAAATGTGACAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACT}$ CACTTGGATGGTCACAAGGTACATATTTCCCGGGATAAGATCACCAGGCCAGGAGCGAAGCT ATGGAAGAAAGGGGAAGGGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAA TCACTTTTGATGTGGATTTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAAA ${\tt CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTATACAATGGACTGCAAGGATAT}{{\tt TGA}{\tt GAGTG}}$ TCATCATGAAATGAATAAGAGGGCTTAAGAATTTGTCCATTTGCATTCGGAAAAGAATGACC AGCAAAAGGTTTACTAATACCTCTCCCTTTGGGGATTTAATGTCTGGTGCTGCCGCCTGAGT TTCAAGAATTAAAGCTGCAAGAGGACTCCAGGAGCAAAAGAAACACAATATAGAGGGTTGGA GTTGTTAGCAATTTCAAAATGCCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTTG TTATTTTTA

පිහි / 310 · FIGURE 85

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRSASIKDIKKAYRKLALQLHPDRNPDDPQ
AQEKFQDLGAAYEVLSDSEKRKQYDTYGEEGLKDGHQSSHGDIFSHFFGDFGFMFGGTPRQQ
DRNIPRGSDIIVDLEVTLEEVYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQ
MTQEVVCDECPNVKLVNEERTLEVEIEPGVRDGMEYPFIGEGEPHVDGEPGDLRFRIKVVKH
PIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVHISRDKITRPGAKLWKKGEGLPNFD
NNNIKGSLIITFDVDFPKEQLTEEAREGIKQLLKQGSVQKVYNGLQGY

FIGURE 86

TGGGACCAGGGAACCCCGGGCCCCCCGGTGGAGNGCCTAACAGGCCGGTGGNTGCGACCGAA
GCGGCGGGCGGAGGAGGTTTTGAGGATTTTTGGAACAGGACCCGGACAGAGGAACCATGGTT
CCGCAGAACNTGAGCACNTTTTGCCTGTTGNTGNTATACTTCATCGGGGCGGTGATTGCCGG
ACGAGATTTNTATAAGATTTTGGGGTGCCTNGAAGTGCCTTNTATAAAAGGATATTAAAAAGG
CCTATAGGAAACTAGCCCTGCAGNTTTATCCCGACCGGAACCCTGATGATCCACAAGCCCAG
GAGAAATTCCAGGATTTGGGTGCTTCATGAGGTTNTGTCAGATAGTGAGAAACGGAAACA
GTACGATAATTATGGTGAAGAAGGATTAAAAGATGGTNATCAGAGCTCCCATGGAGACATTT
TTTCACACTTNTTTGGGGATTTTGGTTTCATGTTTGGAGGAACCCCTNGTCAGCAAGACAGA
AATATTCCAAGAG

GGCACGAGGCGGGGCAGTCGCGGGATGCGCCCGGGAGCCACAGCCTGAGGCCCTCAGGT CTCTGCAGGTGTCGTGGAGGAACCTAGCACCTGCCATCCTCTTCCCCAATTTGCCACTTCCA AGACTGTGGTGATTGTTGCCATAGGTGTGCTGGCCACCATCTTTCTGGCTTCGTTTGCAGCC TTGGTGCTGCTGCAGCGCAGCGCTACTGCCGGCCGCGAGACCTGCTGCAGCGCTATGATTC TAAGCCCATTGTGGACCTCATTGGTGCCATGGAGACCCAGTCTGAGCCCTCTGAGTTAGAAC TGGACGATGTCGTTATCACCAACCCCCACATTGAGGCCATTCTGGAGAATGAAGACTGGATC GAAGATGCCTCGGGTCTCATGTCCCACTGCATTGCCATCTTGAAGATTTGTCACACTCTGAC AGAGAAGCTTGTTGCCATGACAATGGGCTCTGGGGCCAAGATGAAGACTTCAGCCAGTGTCA GCGACATCATTGTGGTGGCCAAGCGGATCAGCCCCAGGGTGGATGATGTTGTGAAGTCGATG TCACCTGGTGCTGACAAGGAATGCCTGCCATCTGACGGGAGGCCTGGACTGGATTGACC AGTCTCTGTCGGCTGCTGAGGAGCATTTGGAAGTCCTTCGAGAAGCAGCCCTAGCTTCTGAG ${\tt CCAGATAAAGGCCTCCCAGGCCCTGAAGGCTTCCTGCAGGAGCAGTCTGCAATT} {\color{red}{\bf TAG}} {\tt TGCCT}$ ACAGGCCAGCAGCTAGCCATGAAGGCCCCTGCCGCCATCCCTGGATGGCTCAGCTTAGCCTT CTACTTTTCCTATAGAGTTAGTTGTTCTCCACGGCTGGAGAGTTCAGCTGTGTGCATAG TAAAGCAGGAGATCCCCGTCAGTTTATGCCTCTTTTGCAGTTGCAAACTGTGGCTGGTGAGT GGCAGTCTAATACTACAGTTAGGGGAGATGCCATTCACTCTCTGCAAGAGGAGTATTGAAAA CTGGTGGACTGTCAGCTTTATTTAGCTCACCTAGTGTTTTCAAGAAAATTGAGCCACCGTCT AAGAAATCAAGAGGTTTCACATTAAAATTAGAATTTCTGGCCTCTCTCGATCGGTCAGAATG GGTCCCTGAGGCGTCTCGCGTCTCCCCTTGCAGGTTTGGAGCTGAGGAACT ACAAAGTTGATGATTTCTTTTTTTTTTTTTTTTTCCTGCAATTTTACCTAGCTACCACTAGGTG

FIGURE 88

METVVIVAIGVLATIFLASFAALVLVCRQRYCRPRDLLQRYDSKPIVDLIGAMETQSEPSEL ELDDVVITNPHIEAILENEDWIEDASGLMSHCIAILKICHTLTEKLVAMTMGSGAKMKTSAS VSDIIVVAKRISPRVDDVVKSMYPPLDPKLLDARTTALLLSVSHLVLVTRNACHLTGGLDWI DQSLSAAEEHLEVLREAALASEPDKGLPGPEGFLQEQSAI

GCTTCATTTCTCCCGACTCAGCTTCCCACCCTGGGCTTTCCGAGGTGCTTTCGCCGCTGTCC $\verb|CCACCACTGCAGCC| \textbf{ATG} \\ \texttt{ATCTCCTTAACGGACACGCAGAAAATTGGAATGGGATTAACAGGA| \\ \\ \texttt{CCACCACTGCAGCC} \\ \textbf{ATG} \\ \texttt{ATCTCCTTAACGGACACGCAGAAAATTGGAATGGGATTAACAGGA| \\ \textbf{ATGTCAGGACACGCAGAAAATTGGAATGGGATTAACAGGA| \\ \textbf{ATGTCAGAGACACGCAGAAAATTGGAATGGGATTAACAGGA| \\ \textbf{ATGTCAGAGACACGCAGAAAATTGGAATGGGATTAACAGGA| \\ \textbf{ATGTCAGAGACACGCAGAAAATTGGAATGGGATTAACAGGA| \\ \textbf{ATGTCAGAGACACGCAGAAAATTGGAATGGGATTAACAGGAACACGCAGAAAATTGGAATGGGATTAACAGGAACACGCAGAAAATTGGAATGGAATGGGATTAACAGGAACACGCAGAAAATTGGAATGAATGGAATGGAATGGAATGGAATGGAATGGAATGGAATGAA$ TTTGGAGTGTTTTTCCTGTTCTTTGGAATGATTCTCTTTTTTGACAAAGCACTACTGGCTAT TCTTCTTCCAAAAACATAAAATGAAAGCTACAGGTTTTTTTCTGGGTGGTGTATTTGTAGTC CTTATTGGTTGGCCTTTGATAGGCATGATCTTCGAAATTTATGGATTTTTTCTCTTGTTCAG GGGCTTCTTTCCTGTCGTTGTTGGCTTTATTAGAAGAGTGCCAGTCCTTGGATCCCTCCTAAAT TTACCTGGAATTAGATCATTTGTAGATAAAGTTGGAGAAAGCAACAATATGGTA<u>TAA</u>CAACA GCACAAAATTAAATTACATGAAATAGCTTGTAATGTTCTTTACAGGAGTTTAAAACGTATAG CCTACAAAGTACCAGCAGCAAATTAGCAAAGAAGCAGTGAAAACAGGCTTCTACTCAAGTGA ACTAAGAAGTCAGCAAGCAAACTGAGAGAGGTGAAATCCATGTTAATGATGCTTAAGAA ACTCTTGAAGGCTATTTGTGTTTTTTCCACAATGTGCGAAACTCAGCCATCCTTAGAGAA $\tt CTGTGGTGCCTGTTTCTTTTTTTTTTTTGAAGGCTCAGGAGCATCCATAGGCATTTGCT$ TTTTAGAAGTGTCCACTGCAATGGCAAAAATATTTCCAGTTGCACTGTATCTCTGGAAGTGA ${\tt TGCATGAATTCGATTGGATTGTGTCATTTTAAAGTATTAAAACCAAGGAAACCCCAATTTTG}$ ATGTATGGATTACTTTTTTTTTGNGCNCAGGGCC

MISLTDTQKIGMGLTGFGVFFLFFGMILFFDKALLAIGNVLFVAGLAFVIGLERTFRFFFQK HKMKATGFFLGGVFVVLIGWPLIGMIFEIYGFFLLFRGFFPVVVGFIRRVPVLGSLLNLPGI RSFVDKVGESNNMV

Important features:

Transmembrane domains:

amino acids 12-30 (typeII), 33-52, 69-89 and 93-109

N-myristoylation sites.

amino acids 11-16, 51-56 and 116-121

Aminoacyl-transfer RNA synthetases class-II protein. amino acids 49-59

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FIGURE 92

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAA $\tt CTGTGGGTAGTTATTTATTTCTGAATAAGAGCGTCCACGCATC \underline{\textbf{ATG}} \texttt{GACCTCGCGGGACTGC}$ TGAAGTCTCAGTTCCTGTGCCACCTGGTCTTCTGCTACGTCTTTATTGCCTCAGGGCTAATC ATCAACACCATTCAGCTCTTCACTCTCCTCCTCTGGCCCATTAACAAGCAGCTCTTCCGGAA GATCAACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGATGCTGCTGGAGTGGTGGT GCCATCGTGGTTCTCAACCACAAGTTTGAAATTGACTTTCTGTGTGGCTGGAGCCTGTCCGA TTATCGGCTGGATGTGGTACTTCACCGAGATGGTCTTCTGTTCGCGCAAGTGGGAGCAGGAT CGCAAGACGGTTGCCACCAGTTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTTTCCT GATTCACTGTGAGGGCACACGGTTCACGGAGAAGAAGCATGAGATCAGCATGCAGGTGGCCC GGGCCAAGGGGCTGCCTCGCCTCAAGCATCACCTGTTGCCACGAACCAAGGGCTTCGCCATC ACCGTGAGGAGCTTGAGAAATGTAGTTTCAGCTGTATATGACTGTACACTCAATTTCAGAAA TTAGGAGGATCCCACTGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCAC AAGCTCTACCAGGAGAAGGATGCCTTTCAGGAGGAGTACTACAGGACGGCACCTTCCCAGA GACGCCCATGGTGCCCCCCGGCGCCCCTGGACCCTCGTGAACTGGCTGTTTTGGGCCTCGC TGGTGCTCTACCCTTTCTTCCAGTTCCTGGTCAGCATGATCAGGAGCGGGTCTTCCCTGACG **GACTCAGGGAGGTGTCACCATCCGAAGGGAACCTTGGGGAACTGGTGGCCTCTGCATATCCT** CCTTAGTGGGACACGGTGACAAAGGCTGGGTGAGCCCCTGCTGGGCACGGCGGAAGTCACGA CCTCTCCAGCCAGGGAGTCTGGTCTCAAGGCCGGATGGGGAGGAAGATGTTTTGTAATCTTT TGTGTGGTGAGTGTGAACTTTGTTCTGTGATCATAGAAAGGGTATTTTAGGCTGCAGGGGAG GGCAGGGCTGGGGACCGAAGGGGACAAGTTCCCCTTTCATCCTTTGGTGCTGAGTTTTCTGT AACCCTTGGTTGCCAGAGATAAAGTGAAAAGTGCTTTAGGTGAGATGACTAAATTATGCCTC

MDLAGLLKSQFLCHLVFCYVFIASGLIINTIQLFTLLLWPINKQLFRKINCRLSYCISSQLV
MLLEWWSGTECTIFTDPRAYLKYGKENAIVVLNHKFEIDFLCGWSLSERFGLLGGSKVLAKK
ELAYVPIIGWMWYFTEMVFCSRKWEQDRKTVATSLQHLRDYPEKYFFLIHCEGTRFTEKKHE
ISMQVARAKGLPRLKHHLLPRTKGFAITVRSLRNVVSAVYDCTLNFRNNENPTLLGVLNGKK
YHADLYVRRIPLEDIPEDDDECSAWLHKLYQEKDAFQEEYYRTGTFPETPMVPPRRPWTLVN
WLFWASLVLYPFFQFLVSMIRSGSSLTLASFILVFFVASVGVRWMIGVTEIDKGSAYGNSDS
KQKLND

FIGURE 94

 $\tt CTGAGGCGGTAGC \underline{ATG} GAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTTGTGCTCG$ GCGCACTCGCTTTCCAGCACCTCAACACGGACTCGGACACGGAAGGTTTTCTTCTTGGGGAA GTAAAAGGTGAAGCCAAGAACAGCATTACTGATTCCCAAATGGATGATGTTGAAGTTGTTTA TACAATTGACATTCAGAAATATATTCCATGCTATCAGCTTTTTAGCTTTTATAATTCTTCAG GCGAAGTAAATGAGCAAGCACTGAAGAAAATATTATCAAATGTCAAAAAGAATGTGGTAGGT AAACTTGCAGGAGCATTTTTCAAACCAAGACCTTGTTTTTCTGCTATTAACACCAAGTATAA TAACAGAAAGCTGCTCTACTCATCGACTGGAACATTCCTTATATAAACCTCAAAAAGGACTT TTTCACAGGGTACCTTTAGTGGTTGCCAATCTGGGCATGTCTGAACAACTGGGTTATAAAAC TGTATCAGGTTCCTGTATGTCCACTGGTTTTAGCCGAGCAGTACAAACACACAGCTCTAAAT TTTTTGAAGAAGATGGATCCTTAAAGGAGGTACATAAGATAAATGAAATGTATGCTTCATTA CAAGAGGAATTAAAGAGTATATGCAAAAAAGTGGAAGACAGTGAACAAGCAGTAGATAAACT AGTAAAGGATGTAAACAGATTAAAACGAGAAATTGAGAAAAGGAGAGGAGCACAGATTCAGG CAGCAAGAGAAGAACATCCAAAAAGACCCTCAGGAGAACATTTTTCTTTGTCAGGCATTA CGGACCTTTTTTCCAAATTCTGAATTTCTTCATTCATGTGTTATGTCTTTAAAAAATAGACA TGTTTCTAAAAGTAGCTGTAACTACAACCACCATCTCGATGTAGTAGACAATCTGACCTTAA TGGTAGAACACACTGACATTCCTGAAGCTAGTCCAGCTAGTACACCACAAATCATTAAGCAT AAAGCCTTAGACTTAGATGACAGATGGCAATTCAAGAGATCTCGGTTGTTAGATACACAAGA CAAACGATCTAAAGCAAATACTGGTAGTAGTAACCAAGATAAAGCATCCAAAATGAGCAGCC CAGAAACAGATGAAGAATTGAAAAGATGAAGGGTTTTGGTGAATATTCACGGTCTCCTACA TTCTATTGTTTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTCAC CTGTTTGCAGTAATACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTCAAAC ATCAGATGCTTTTATTTCCAAACCTTTTTTTCACCTTTCACTAAGTTGTTGAGGGGAAGGCT TACACAGACACATTCTTTAGAATTGGAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAA TGGGCAACGTATTGAGACCATGTCTATTAAAAAATAAAATGGAAAAGCAAGAATAGCCTTAT TTTCAAAATATGGAAAGAAATTTATATGAAAATTTATCTGAGTCATTAAAATTCTCCTTAAG TGATACTTTTTTAGAAGTACATTATGGCTAGAGTTGCCAGATAAAATGCTGGATATCATGCA

FIGURE 95

MEGESTSAVLSGFVLGALAFQHLNTDSDTEGFLLGEVKGEAKNSITDSQMDDVEVVYTIDIQ
KYIPCYQLFSFYNSSGEVNEQALKKILSNVKKNVVGWYKFRRHSDQIMTFRERLLHKNLQEH
FSNQDLVFLLLTPSIITESCSTHRLEHSLYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSC
MSTGFSRAVQTHSSKFFEEDGSLKEVHKINEMYASLQEELKSICKKVEDSEQAVDKLVKDVN
RLKREIEKRRGAQIQAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVSKSS
CNYNHHLDVVDNLTLMVEHTDIPEASPASTPQIIKHKALDLDDRWQFKRSRLLDTQDKRSKA
NTGSSNQDKASKMSSPETDEEIEKMKGFGEYSRSPTF

FIGURE 96

CCGCGGCGCCTGCCACCCTTCCCTCCTTCCCCGCGTCCCCGCCTCGCCGGCCAGTCAGCTTG CGCGCCGCCTCCACGCCCTCCTTCTCCCCTGGCCCGGGCGCCCTGGCACCGGGGACCGTTGCCT GACGCGAGGCCCAGCTCTACTTTTCGCCCCGCGTCTCCTCCGCCTGCTCGCCTCTTCCACCA ACTCCAACTCCTTCTCCCTCCAGCTCCACTCGCTAGTCCCCGACTCCGCCAGCCCTCGGCCC GCTGCCGTAGCGCCGCTCCCGTCCCGAAAGGTGGGAACGCGTCCGCCCCGGCCCGCA $CC\underline{ATG}$ GCACGGTTCGGCTTGCCCGCGCTTCTCTGCACCCTGGCAGTGCTCAGCGCCGCGCTG CTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGGAAGTGCGACGTCTTTACGTGTCCAAAGG CTTCAACAAGAACGATGCCCCCTCCACGAGATCAACGGTGATCATTTGAAGATCTGTCCCC AGGGTTCTACCTGCTGCTCTCAAGAGATGGAGGAGAAGTACAGCCTGCAAAGTAAAGATGAT TTCAAAAGTGTGGTCAGCGAACAGTGCAATCATTTGCAAGCTGTCTTTGCTTCACGTTACAA GAAGTTTGATGAATTCTTCAAAGAACTACTTGAAAATGCAGAGAAATCCCTGAATGATATGT TTGTGAAGACATATGGCCATTTATACATGCAAAATTCTGAGCTATTTAAAGATCTCTTCGTA GAGTTGAAACGTTACTACGTGGTGGGAAATGTGAACCTGGAAGAAATGCTAAATGACTTCTG GGCTCGCCTCCTGGAGCGGATGTTCCGCCTGGTGAACTCCCAGTACCACTTTACAGATGAGT ATCTGGAATGTGTGAGCAAGTATACGGAGCAGCTGAAGCCCTTCGGAGATGTCCCTCGCAAA TTGAAGCTCCAGGTTACTCGTGCTTTTGTAGCAGCCCGTACTTTCGCTCAAGGCTTAGCGGT TGCGGGAGATGTCGTGAGCAAGGTCTCCGTGGTAAACCCCACAGCCCAGTGTACCCATGCCC TGTTGAAGATGATCTACTGCTCCCACTGCCGGGGTCTCGTGACTGTGAAGCCATGTTACAAC TACTGCTCAAACATCATGAGAGGCTGTTTGGCCAACCAAGGGGATCTCGATTTTGAATGGAA CAATTTCATAGATGCTATGCTGATGGTGGCAGAGGGCTAGAGGGTCCTTTCAACATTGAAT CGGTCATGGATCCCATCGATGTGAAGATTTCTGATGCTATTATGAACATGCAGGATAATAGT GTTCAAGTGTCTCAGAAGGTTTTCCAGGGATGTGGACCCCCCAAGCCCCTCCCAGCTGGACG AATTTCTCGTTCCATCTCTGAAAGTGCCTTCAGTGCTCGCTTCAGACCACATCACCCCGAGG AACGCCCAACCACAGCAGCTGGCACTAGTTTGGACCGACTGGTTACTGATGTCAAGGAGAAA CTGAAACAGGCCAAGAAATTCTGGTCCTCCCTTCCGAGCAACGTTTGCAACGATGAGAGGAT GGCTGCAGGAAACGGCAATGAGGATGACTGTTGGAATGGGAAAGGCAAAAGCAGGTACCTGT TTGCAGTGACAGGAAATGGATTAGCCAACCAGGGCAACAACCCAGAGGTCCAGGTTGACACC AGCAAACCAGACATACTGATCCTTCGTCAAATCATGGCTCTTCGAGTGATGACCAGCAAGAT GAAGAATGCATACAATGGGAACGACGTGGACTTCTTTGATATCAGTGATGAAAGTAGTGGAG AAGGAAGTGGAAGTGGCTGTGAGTATCAGCAGTGCCCTTCAGAGTTTGACTACAATGCCACT GACCATGCTGGGAAGAGTGCCAATGAGAAAGCCGACAGTGCTGGTGTCCCTGGGGCACA TCTCAAACTCTGAGAAAAAGTGTTCATCAAAAAGTTAAAAGGCACCAGTTATCACTTTTCTA CCATCCTAGTGACTTTGCTTTTTAAATGAATGGACAACAATGTACAGTTTTTACTATGTGGC CACTGGTTTAAGAAGTGCTGACTTTGTTTTCTCATTCAGTTTTGGGAGGAAAAGGGACTGTG CATTGAGTTGGTTCCTGCTCCCCAAACCATGTTAAACGTGGCTAACAGTGTAGGTACAGAA CTATAGTTAGTTGTGCATTTGTGATTTTATCACTCTATTATTTGTTTTGTATGTTTTTTTCTC ATTTCGTTTGTGGGTTTTTTTTTCCAACTGTGATCTCGCCTTGTTTCTTACAAGCAAACCAG GGTCCCTTCTTGGCACGTAACATGTACGTATTTCTGAAATATTAAATAGCTGTACAGAAGCA GGTTTTATTTATCATGTTATCTTATTAAAAGAAAAAGCCCAAAAAGC در ب

FIGURE 97

MARFGLPALLCTLAVLSAALLAAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQ
GSTCCSQEMEEKYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFFKELLENAEKSLNDMF
VKTYGHLYMQNSELFKDLFVELKRYYVVGNVNLEEMLNDFWARLLERMFRLVNSQYHFTDEY
LECVSKYTEQLKPFGDVPRKLKLQVTRAFVAARTFAQGLAVAGDVVSKVSVVNPTAQCTHAL
LKMIYCSHCRGLVTVKPCYNYCSNIMRGCLANQGDLDFEWNNFIDAMLMVAERLEGPFNIES
VMDPIDVKISDAIMNMQDNSVQVSQKVFQGCGPPKPLPAGRISRSISESAFSARFRPHHPEE
RPTTAAGTSLDRLVTDVKEKLKQAKKFWSSLPSNVCNDERMAAGNGNEDDCWNGKGKSRYLF
AVTGNGLANQGNNPEVQVDTSKPDILILRQIMALRVMTSKMKNAYNGNDVDFFDISDESSGE
GSGSGCEYQQCPSEFDYNATDHAGKSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR

FIGURE 98

MKVLISSLLLLLPLMLMSMVSSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRR KFMTVSGLPKKQCPCDHFKGNVKKTRHQRHHRKPNKHSRACQQFLKQCQLRSFALPL

_103/310 FIGURE 100

MAVLVLRLTVVLGLLVLFLTCYADDKPDKPDDKPDDSGKDPKPDFPKFLSLLGTEIIENAVE FILRSMSRSTGFMEFDDNEGKHSSK

GGACGCCAGCGCAGAGGCTGAGCAGGGAAAAAGCCAGTGCCCCAGCGGAAGCACAGCT ${\tt CAGAGCTGGTCTGCC} \underline{\textbf{ATG}} \\ \texttt{GACATCCTGGTCCCACTCCTGCAGCTGCTGGTGCTGCTTCTTAC}$ CCTGCCCCTGCACCTCATGGCTCTGCTGGGCTGCTGGCAGCCCCTGTGCAAAAGCTACTTCC CCTACCTGATGGCCGTGCTGACTCCCAAGAGCCAACCGCAAGATGGAGAGCAAGAACGGGAG $\tt CTCTTCAGCCAGATAAAGGGGCTTACAGGAGCCTCCGGGAAAGTGGCCCTACTGGAGCTGGG$ CTGCGGAACCGGAGCCAACTTTCAGTTCTACCCACCGGGCTGCAGGGTCACCTGCCTAGACC CAAATCCCCACTTTGAGAAGTTCCTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATAT GGTGGTCTGCACTCTGTGCTGTGCAGAGCCCAAGGAAGGTCCTGCAGGAGGTCC GGAGAGTACTGAGACCGGGAGGTGTGCTCTTTTTCTGGGAGCATGTGGCAGAACCATATGGA AGCTGGGCCTTCATGTGGCAGCAAGTTTTCGAGCCCACCTGGAAACACATTGGGGATGGCTG CTGCCTCACCAGAGAGCCTGGAAGGATCTTGAGAACGCCCAGTTCTCCGAAATCCAAATGG AACGACAGCCCCTCCCTTGAAGTGGCTACCTGTTGGGCCCCACATCATGGGAAAGGCTGTC AAACAATCTTTCCCAAGCTCCAAGGCACTCATTTGCTCCTTCCCCAGCCTCCAATTAGAACA ${\tt AGCCACCCACCAGCCTATCTATCTTCCACTGAGAGGGACC\underline{{\tt TAG}}{\tt CAGAATGAGAGAGACATT}$ CATGTACCACCTACTAGTCCCTCTCTCCCCAACCTCTGCCAGGGCAATCTCTAACTTCAATC CCGCCTTCGACAGTGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGGAAACACTAGGACCC TGTTGTATCCTCAACTGCAAGTTTCTGGACTAGTCTCCCAACGTTTGCCTCCCAATGTTGTC ${\tt CCTTTCCTTCGTTCCCATGGTAAAGCTCCTCTCGCTTTCCTCCTGAGGCTACACCCATGCGT}$ CTCTAGGAACTGGTCACAAAAGTCATGGTGCCTGCATCCCTGCCAAGCCCCCTGACCCTCT CTCCCCACTACCACCTTCTTCCTGAGCTGGGGGCACCAGGGAGAATCAGAGATGCTGGGGAT **AACCACG**

MDILVPLLQLLVLLTLPLHLMALLGCWQPLCKSYFPYLMAVLTPKSNRKMESKKRELFSQI KGLTGASGKVALLELGCGTGANFQFYPPGCRVTCLDPNPHFEKFLTKSMAENRHLQYERFVV APGEDMRQLADGSMDVVVCTLVLCSVQSPRKVLQEVRRVLRPGGVLFFWEHVAEPYGSWAFM WQQVFEPTWKHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLPVGPHIMGKAVKQSFP SSKALICSFPSLQLEQATHQPIYLPLRGT

GTGGGATTTATTTGAGTGCAAGATCGTTTTCTCAGTGGTGGTGGAAGTTGCCTCATCGCAGG CAGATGTTGGGGCTTTGTCCGAACAGCTCCCCTCTGCCAGCTTCTGTAGATAAGGGTTAAAA ACTAATATTTATATGACAGAAGAAAAAGATGTCATTCCGTAAAGTAAACATCATCTTGG TCCTGGCTGTTGCTCTTCTTACTGGTTTTGCACCATAACTTCCTCAGCTTGAGCAGTTTG TTAAGGAATGAGGTTACAGATTCAGGAATTGTAGGGCCTCAACCTATAGACTTTGTCCCAAA TGCTCTCCGACATGCAGTAGATGGGAGACAAGAGGGAGATTCCTGTGGTCATCGCTGCATCTG AAGACAGGCTTGGGGGGGCCATTGCAGCTATAAACAGCATTCAGCACAACACTCGCTCCAAT GTGATTTTCTACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGTCCTGGCTCAACAG AAGTAAAGGAGGATCCTGACCAGGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTAC TTGCCAATTCTGGTTCCCAGCGCAAAGAAGGCCATATACATGGATGATGTAATTGTGCA AGGTGATATTCTTGCCCTTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAG AAGATTGTGATTCAGCCTCTACTAAAGTTGTCATCCGTGGAGCAGGAAACCAGTACAATTAC ATTGGCTATCTTGACTATAAAAAGGAAAGAATTCGTAAGCTTTCCATGAAAGCCAGCACTTG CTCATTTAATCCTGGAGTTTTTGTTGCAAACCTGACGGAATGGAAACGACAGAATATAACTA ACCAACTGGAAAAATGGATGAAACTCAATGTAGAAGAGGGACTGTATAGCAGAACCCTGGCT GGTAGCATCACAACACCTCCTCTGCTTATCGTATTTTATCAACAGCACTCTACCATCGATCC TATGTGGAATGTCCGCCACCTTGGTTCCAGTGCTGGAAAACGATATTCACCTCAGTTTGTAA AGGCTGCCAAGTTACTCCATTGGAATGGACATTTGAAGCCATGGGGAAGGACTGCTTCATAT ACTGATGTTTGGGAAAAATGGTATATTCCAGACCCAACAGGCAAATTCAACCTAATCCGAAG GAAGTCCTGGAAGATAGCATGCATGGGAAGTAACAGTTGCTAGGCTTCAATGCCTATCGGTA GCAAGCCATGGAAAAAGATGTCTCAGCTAGGTAAAGATGACAAACTGCCCTGTCTGGCAGTC AGCTTCCCAGACAGACTATAGACTATAAATATGTCTCCATCTGCCTTACCAAGTGTTTTCTT ACATTTTTC

FIGURE 105

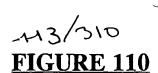
MSFRKVNIIILVLAVALFLLVLHHNFLSLSSLLRNEVTDSGIVGPQPIDFVPNALRHAVDGR QEEIPVVIAASEDRLGGAIAAINSIQHNTRSNVIFYIVTLNNTADHLRSWLNSDSLKSIRYK IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVIVQGDILALYNT ALKPGHAAAFSEDCDSASTKVVIRGAGNQYNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA NLTEWKRQNITNQLEKWMKLNVEEGLYSRTLAGSITTPPLLIVFYQQHSTIDPMWNVRHLGS SAGKRYSPQFVKAAKLLHWNGHLKPWGRTASYTDVWEKWYIPDPTGKFNLIRRYTEISNIK

CGACGCTCTAGCGGTTACCGCTGCGGGCTGGCCGGCTAGTGGGGCTGCCGCCGCTGCCACG TGGGCTCCGGGGCCTGCGCGGGCGGGCGGGCTGGGCGGGCGGGCGGGCTGCA TCCGCATCTCCTCCATCGCCTGCAGTAAGGGCGGCCGCGGCGAGCCTTTGAGGGGAACGACT TGTCGGAGCCCTAACCAGGGGTGTCTCTGAGCCTGGTGGGATCCCCGGAGCGTCACATCACT TTCCGATCACTTCAAAGTGGTTAAAAACTAATATTTATATGACAGAAGAAAAAGATGTCATT CCGTAAAGTAAACATCATCATCTTGGTCCTGGGCTGTTGCTCTTCTTACTGGTTTTGCAC CATAACTTCCTCAGCTTGAGGCAGTTTGTTAAGGAATGAGGTTACAGATTCAGGAATTGTAG GGCCTCAACCTATAGGACTTTGTCCCAAATGCTCTCCGACATGCAGTAGATGGGAGACAAGA GGAGATTCCTGTGGTCATCGCTGCATCTGAAGACAGGCTTGGGGGGGCCATTGCAGCTATAA ACAGCATTCAGCACAACACTCGCTCCAATGTGATTTTCTACATTGTTACTCTCAACAATACA GCAGACCATCTCCGGTCCTGGGCTCAACAGTGATTCCCTGAAAAGCATCAGATACAAAATTG TCAATTTTGACCCTAAACTTTTGGAAGGAAAAGTAAAGGAGGATCCTGACCAGGGGGAATCC ATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGGTTCCCAGCGCAAAGAAGA CCATATACATGGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTACAATACAGCA CTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTCAGCCTCTACTAAAGTTGT CATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTATCTTGACTATAAAAAGGAAAGAA TTCGTAAGCTTTCCATGAAAGCCAGCACTTGCTCATTTAATCCTGGAGTTTTTGTTGCAAAC CTGACGGAATGGAAACGACAGAATATAACTAACCAACTGGAAAAATGGATGAAACTCAATGT AGAAGAGGGACTGTATAGCAGAACCCTGGCTGGTAGCATCACAACACCTCCTCTGCTTATCG TATTTTATCAACAGCACTCTACCATCGATCCTATGTGGAATGTCCGCCACCTTGGTTCCAGT GCTGGAAAACGATATTCACCTCAGTTTGTAAAGGCTGCCAAGTTACTCCATTGGAATGGACA TTTGAAGCCATGGGGAAGGACTGCTTCATATACTGATGTTTGGGGAAAAATGGTATATTCCA GACCCAACAGGCAAATTCAACCTAATCCGAAGATATACCGAGATCTCAAACATAAAGTGAAA CAGAATTTGAACTGTAAGCAAGCATTTCTCAGGAAGTCCTGGAAGATAGCATGCGTGGGAAG TAACAGTTGCTAGGCTTCAATGCCTATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAG ATGTCTCCATCTGCCTTACCAAGTGTTTTCTTACTACAATGCTGAATGACTGGAAAGAAGAA CTGATATGGCTAGTTCAGCTAGCTGGTACAGATAATTCAAAACTGCTGTTGGTTTTAATTTT AAAAA

FIGURE 108

 ${\tt MGAAISQGALIAIVCNGLVGFLLLLWVILCWACHSRLPTLTLSLNPVPTPALAPVLRRPHH} \\ {\tt PRSPAMKAATCCSPEGPWPSLEPRT}$

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GTTTGAATTCCTTCAACTATACCCACAGTCCAAAAGCAGACTCACTGTGTCCCAGGCTACCA GTTCCTCCAAGCAAGTCATTTCCCTTATTTAACCGATGTGTCCCTCAAACACCTGAGTGCTA CTCCCTATTTGCATCTGTTTTGATAAATGATGTTGACACCCTCCACCGAATTCTAAGTGGAA TCATGTCGGGAAGAGATACAATCCTTGGCCTGTGTATCCTCGCATTAGCCTTGTCTTTGGCC **ATGATGTTTACCTTCAGATTCATCACCACCCTTCTGGTTCACATTTTCATTTCATTGGTTAT** TTTGGGATTGTTGTCTGCGGTGTTTTATGGTGGCTGTATTATGACTATACCAACGACC TCCACAGGCATCACGGCAGTGCTGCTCGTCTTGATTTTTGTTCTCAGAAAGAGAATAAAATT GACAGTTGAGCTTTTCCAAATCACAAATAAAGCCATCAGCAGTGCTCCCTTCCTGCTGTTCC AGCCACTGTGGACATTTGCCATCCTCATTTTCTTCTGGGTCCTCTGGGTGGCTGTGCTGCTG AGCCTGGGAACTGCAGGAGCTGCCCAGGTTATGGAAGGCGGCCAAGTGGAATATAAGCCCCT TTCGGGCATTCGGTACATGTGGTCGTACCATTTAATTGGCCTCATCTGGACTAGTGAATTCA TCCTTGCGTGCCAGCAAATGACTATAGCTGGGGCAGTGGTTACTTGTTATTTCAACAGAAGT AAAAATGATCCTCCTGATCATCCCATCCTTTCGTCTCTCCATTCTCTTCTTCTACCATCA **AGGAACCGTTGTGAAAGGGTCATTTTTAATCTCTGTGGTGAGGATTCCGAGAATCATTGTCA** TGTACATGCAAAACGCACTGAAAGAACAGCAGCATGGTGCATTGTCCAGGTACCTGTTCCGA TGCTGCTACTGCTGTTTCTGGTGTCTTGACAAATACCTGCTCCATCTCAACCAGAATGCATA TACTACAACTGCTATTAATGGGACAGATTTCTGTACATCAGCAAAAGATGCATTCAAAATCT TGTCCAAGAACTCAAGTCACTTTACATCTATTAACTGCTTTGGAGACTTCATAATTTTTCTA GGAAAGGTGTTAGTGGTGTTTTCACTGTTTTTGGAGGACTCATGGCTTTTAACTACAATCG GGCATTCCAGGTGTGGGCAGTCCCTCTGTTATTGGTAGCTTTTTTTGCCTACTTAGTAGCCC ATAGTTTTTTATCTGTGTTTGAAACTGTGCTGGATGCACTTTTCCTGTGTTTTGCTGTTGAT CTGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTTATGGATCAAGAATTTCTGAGTTT CGTAAAAAGGAGCAACAAATTAAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGA GGAAAACATTTCCTTCTAAGAGCCATTTACAGAATAGAAGATGAGACCACTAGAGAAAAGTT AGTGAATTTTTTTTTAAAAGACCTAATAAACCCTATTCTTCCTCAAAA

MSGRDTILGLCILALALSLAMMFTFRFITTLLVHIFISLVILGLLFVCGVLWWLYYDYTNDL
SIELDTERENMKCVLGFAIVSTGITAVLLVLIFVLRKRIKLTVELFQITNKAISSAPFLLFQ
PLWTFAILIFFWVLWVAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHLIGLIWTSEFI
LACQQMTIAGAVVTCYFNRSKNDPPDHPILSSLSILFFYHQGTVVKGSFLISVVRIPRIIVM
YMQNALKEQQHGALSRYLFRCCYCCFWCLDKYLLHLNQNAYTTTAINGTDFCTSAKDAFKIL
SKNSSHFTSINCFGDFIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLLVAFFAYLVAH
SFLSVFETVLDALFLCFAVDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHSLRN
EEGTELQAIVR

GTTCGATTAGCTCCTCTGAGAAGAAGAGAAAAGGTTCTTGGACCTCTCCCTGTTTCTTCCTT TGTGGTGAAAATTTTTTGAAAAAAAAATTGCCTTCTTCAAACAAGGGTGTCATTCTGATATT TATGAGGACTGTTGTTCTCACTATGAAGGCATCTGTTATTGAAATGTTCCTTGTTTTGCTGG TGACTGGAGTACATTCAAACAAAGAAACGGCAAAGAAGATTAAAAGGCCCAAGTTCACTGTG CCTCAGATCAACTGCGATGTCAAAGCCGGAAAGATCATCGATCCTGAGTTCATTGTGAAATG TCCAGCAGGATGCCAAGACCCCAAATACCATGTTTATGGCACTGACGTGTATGCATCCTACT CCAGTGTGTGTGGCGCTGCCGTACACAGTGGTGTGCTTGATAATTCAGGAGGGAAAATACTT GTTCGGAAGGTTGCTGGACAGTCTGGTTACAAAGGGAGTTATTCCAACGGTGTCCAATCGTT ATCCCTACCACGATGGAGAGATCCTTTATCGTCTTAGAAAGTAAACCCAAAAAGGGTGTAA CCTACCCATCAGCTCTTACATACTCATCATCGAAAAGTCCAGCTGCCCAAGCAGGTGAGACC ACAAAAGCCTATCAGAGGCCACCTATTCCAGGGACAACTGCACAGCCGGTCACTCTGATGCA GCTTCTGGCTGTCACTGTAGCTGTGGCCACCCCCACCACCTTGCCAAGGCCATCCCCTTCTG CTGCTTCTACCACCAGCATCCCCAGACCACAATCAGTGGGCCACAGGAGCCAGGAGATGGAT CTCTGGTCCACTGCCACCTACACAAGCAGCCAAAACAGGCCCAGAGCTGATCCAGGTATCCA AAGGCAAGATCCTTCAGGAGCTGCCTTCCAGAAACCTGTTGGAGCGGATGTCAGCCTGGGAC TTGTTCCAAAAGAAGAATTGAGCACACAGTCTTTGGAGCCAGTATCCCTGGGAGATCCAAAC TGCAAAATTGACTTGTCGTTTTTAATTGATGGGAGCACCAGCATTGGCAAACGGCGATTCCG **AATCCAGAAGCAGCTCCTGGCTGATGTTGCCCAAGCTCTTGACATTGGCCCTGCCGGTCCAC** AATTCTCGAGATCTGAAGACAGCCATAGAGAAAATTACTCAGAGAGGAGGACTTTCTAATGT AGGTCGGGCCATCTCCTTTGTGACCAAGAACTTCTTTTCCAAAGCCAATGGAAACAGAAGCG GGGCTCCCAATGTGGTGGTGATGGTGGATGGCTGGCCCACGGACAAAGTGGAGGAGGCT TCAAGACTTGCGAGAGAGTCAGGAATCAACATTTTCTTCATCACCATTGAAGGTGCTGCTGA AAATGAGAAGCAGTATGTGGTGGAGCCCAACTTTGCAAACAAGGCCGTGTGCAGAACAAACG GCTTCTACTCGCTCCACGTGCAGAGCTGGTTTGGCCTCCACAAGACCCTGCAGCCTCTGGTG AAGCGGGTCTGCGACACTGACCGCCTGGCCTGCAGCAAGACCTGCTTGAACTCGGCTGACAT TGGCTTCGTCATCGACGGCTCCAGCAGTGTGGGGACGGGCAACTTCCGCACCGTCCTCCAGT TTGTGACCAACCTCACCAAAGAGTTTGAGATTTCCGACACGGACACGCGCATCGGGGCCGTG CAGTACACCTACGAACAGCGGCTGGAGTTTGGGTTCGACAAGTACAGCAGCAAGCCTGACAT $\tt CCTCAACGCCATCAAGAGGGTGGGCTACTGGAGTGGTGGCACCAGCACGGGGGCTGCCATCA$ ACTTCGCCCTGGAGCAGCTCTTCAAGAAGTCCAAGCCCAACAAGAGGAAGTTAATGATCCTC ATCACCGACGGGAGGTCCTACGACGACGTCCGGATCCCAGCCATGGCTGCCCATCTGAAGGG AGTGATCACCTATGCGATAGGCGTTGCCTGGGCTGCCCAAGAGGAGCTAGAAGTCATTGCCA CTCACCCCGCCAGAGACCACTCCTTCTTTGTGGACGAGTTTGACAACCTCCATCAGTATGTC CCCAGGATCATCCAGAACATTTGTACAGAGTTCAACTCACAGCCTCGGAACTGAATTCAGAG CAGGCAGAGCACCAGCAAGTGCTGCTTTACTAACTGACGTGTTGGACCACCCCACCGCTTAA TGGGGCACGCACGGTGCATCAAGTCTTGGGCAGGGCATGGAGAAACAAATGTCTTGTTATTA TTCTTTGCCATCATGCTTTTTCATATTCCAAAACTTGGAGTTACAAAGATGATCACAAACGT ATAGAATGAGCCAAAAGGCTACATCATGTTGAGGGTGCTGGAGATTTTACATTTTGACAATT GTTTTCAAAATAAATGTTCGGAATACAGTGCAGCCCTTACGACAGGCTTACGTAGAGCTTTT GTGAGATTTTTAAGTTGTTATTTCTGATTTGAACTCTGTAACCCTCAGCAAGTTTCATTTTT

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FIGURE 113

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPKFTVPQINCDVKAGKIIDPEFIVKC
PAGCQDPKYHVYGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSL
SLPRWRESFIVLESKPKKGVTYPSALTYSSSKSPAAQAGETTKAYQRPPIPGTTAQPVTLMQ
LLAVTVAVATPTTLPRPSPSAASTTSIPRPQSVGHRSQEMDLWSTATYTSSQNRPRADPGIQ
RQDPSGAAFQKPVGADVSLGLVPKEELSTQSLEPVSLGDPNCKIDLSFLIDGSTSIGKRRFR
IQKQLLADVAQALDIGPAGPLMGVVQYGDNPATHFNLKTHTNSRDLKTAIEKITQRGGLSNV
GRAISFVTKNFFSKANGNRSGAPNVVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAE
NEKQYVVEPNFANKAVCRTNGFYSLHVQSWFGLHKTLQPLVKRVCDTDRLACSKTCLNSADI
GFVIDGSSSVGTGNFRTVLQFVTNLTKEFEISDTDTRIGAVQYTYEQRLEFGFDKYSSKPDI
LNAIKRVGYWSGGTSTGAAINFALEQLFKKSKPNKRKLMILITDGRSYDDVRIPAMAAHLKG
VITYAIGVAWAAQEELEVIATHPARDHSFFVDEFDNLHQYVPRIIQNICTEFNSQPRN

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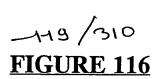
FIGURE 114

CAGGATGAACTGGTTGCAGTGGCTGCTGCTGCGGGGGGCGCTGAGAGGACACGAGCTCTA TGCCTTTCCGGCTGCTCATCCCGCTCGGCCTCCTGTGCGCGCTGCTGCCTCAGCACCATGGT GCGCCAGGTCCCGACGGCTCCGCGCCAGATCCCGCCCACTACAGTTTTTCTCTGACTCTAAT TGATGCACTGGACACCTTGCTGATTTTGGGGAATGTCTCAGAATTCCAAAGAGTGGTTGAAG CGAGTGGTAGGAGGACTCCTGTCTGCTCATCTGCTCTCCAAGAAGGCTGGGGTGGAAGTAGA GGCTGGATGGCCCTGTTCCGGGCCTCTCCTGAGAATGGCTGAGGAGGCGGCCCGAAAACTCC AACCCAGGAGAGCCCCTGTCACCTGTACGGCAGGGATTGGGACCTTCATTGTTGAATTTGC CACCCTGAGCAGCCTCACTGGTGACCCGGTGTTCGAAGATGTGGCCAGAGTGGCTTTGATGC GCCTCTGGGAGAGCCGGTCAGATATCGGGCTGGTCGGCAACCACATTGATGTGCTCACTGGC AAGTGGGTGGCCCAGGACGCAGGCATCGGGGCTGGCGTGGACTCCTACTTTGAGTACTTGGT GAAAGGAGCCATCCTGCTTCAGGATAAGAAGCTCATGGCCATGTTCCTAGAGTATAACAAAG CCATCCGGAACTACACCCGCTTCGATGACTGGTACCTGTGGGTTCAGATGTACAAGGGGACT GTGTCCATGCCAGTCTTCCAGTCCTTGGAGGCCTACTGGCCTGGTCTTCAGAGCCTCATTGG AGACATTGACAATGCCATGAGGACCTTCCTCAACTACTACACTGTATGGAAGCAGTTTGGGG GGCTCCCGGAATTCTACAACATTCCTCAGGGATACACAGTGGAGAAGCGAGAGGGCTACCCA CTTCGGCCAGAACTTATTGAAAGCGCAATGTACCTCTACCGTGCCACGGGGGATCCCACCCT CCTAGAACTCGGAAGAGATGCTGTGGAATCCATTGAAAAAATCAGCAAGGTGGAGTGCGGAT TTGCAACAATCAAAGATCTGCGAGACCACAAGCTGGACAACCGCATGGAGTCGTTCTTCCTG GTCCACCTTCGACGCGGTGATCACCCCCTATGGGGAGTGCATCCTGGGGGGCTGGGGGGTACA TCTTCAACACAGAAGCTCACCCCATCGACCTTGCCGCCCTGCACTGCTGCCAGAGGCTGAAG GAAGAGCAGTGGGAGGTGGAGGACTTGATGAGGGAATTCTACTCTCTCAAACGGAGCAGGTC GAAATTTCAGAAAAACACTGTTAGTTCGGGGCCATGGGAACCTCCAGCAAGGCCAGGAACAC CTTCTCAGCTGCCCCAGTCAGCCCTTCACCTCCAAGTTGGCATTACTGGGACAGGTTTTCCT ${\tt AGACTCCTCA} \underline{{\tt TAA}} {\tt CCACTGGATAATTTTTTTTTTTTTTTTTTTTTTTTTGAGGCTAAACTATAATA}$ AATTGCTTTTGGCTATCATAAAA

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MPFRLLIPLGLLCALLPQHHGAPGPDGSAPDPAHYSFSLTLIDALDTLLILGNVSEFQRVVE
VLQDSVDFDIDVNASVFETNIRVVGGLLSAHLLSKKAGVEVEAGWPCSGPLLRMAEEAARKL
LPAFQTPTGMPYGTVNLLHGVNPGETPVTCTAGIGTFIVEFATLSSLTGDPVFEDVARVALM
RLWESRSDIGLVGNHIDVLTGKWVAQDAGIGAGVDSYFEYLVKGAILLQDKKLMAMFLEYNK
AIRNYTRFDDWYLWVQMYKGTVSMPVFQSLEAYWPGLQSLIGDIDNAMRTFLNYYTVWKQFG
GLPEFYNIPQGYTVEKREGYPLRPELIESAMYLYRATGDPTLLELGRDAVESIEKISKVECG
FATIKDLRDHKLDNRMESFFLAETVKYLYLLFDPTNFIHNNGSTFDAVITPYGECILGAGGY
IFNTEAHPIDLAALHCCQRLKEEQWEVEDLMREFYSLKRSRSKFQKNTVSSGPWEPPARPGT
LFSPENHDQARERKPAKQKVPLLSCPSQPFTSKLALLGQVFLDSS



AAAGTTACATTTCTCTGGAACTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTG GGCAGAAAGGAGGGTGCTTCGGAGCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACA ATTCAGGCTTCGCTGCGACTCAGACCTCCAACATATGCATTCTGAAGAAGATGGCT GAGATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACTGAGTCTACCA ${\tt A} \underline{\textbf{ATG}} \textbf{CAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCTTTTCATGTGGTTTTTCT}$ TCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGA AACAGTGTACTATTCTGTCGAATACCAGGGGGGGTACGAGGCCTGTACACGAGCCACATCT GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTGATGTCACTGATGACATC ACGGCCACTGTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTG GAGCATCCTGAAGCATCCCTTTAATAGAAACTCAACCATCCTTACCCGACCTGGGATGGAGA TCACCAAAGATGGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTC CTTGTGGCCTACTGGAGGAGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGG GGGTATTCCAGTGCACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGA GGAGAGGCCATTCCCCTGGTACTGGCCCTGTTTGCCTTTGTTGGCTTCATGCTGATCCTTGT GGTCGTGCCACTGTTCGTCTGGAAAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCCGTGG TGGTCCTCCCAGACACCTTGAAAATAACCAATTCACCCCAGAAGTTAATCAGCTGCAGAAGG GAGGAGGTGGATGCCTGTGCCACGGCTGTGATGTCTCCTGAGGAACTCCTCAGGGCCTGGAT CTCATAGGTTTGCGGAAGGGCCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACC ATGAGGGACAAGTTGTGTTTCTGTTTTCCGCCACGGACAAGGGATGAGAAGTAGGAAGA GCCTGTTGTCTACAAGTCTAGAAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACAC CTGGGAAAAGTGACTTCATCCCTTCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACC TGTTTCTGGAGAGCAGACATAAATGTATGATGAGAATGATCAAGGACTCTACACACTGGGT GGCTTGGAGAGCCCACTTTCCCAGAATAATCCTTGAGAGAAAAGGAATCATGGGAGCAATGG TGTTGAGTTCACTTCAAGCCCAATGCCGGTGCAGAGGGGAATGGCTTAGCGAGCTCTACAGT AGGTGACCTGGAGGAAGGTCACAGCCACACTGAAAATGGGATGTGCATGAACACGGAGGATC TGTTGGTAAAGTACAGAATTCAGCAAATAAAAAGGGCCACCCTGGCCAAAAGCGGTAAAAAA ΑΑΑΑΑΑΑΑ

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FIGURE 117

MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGE
TVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW
SILKHPFNRNSTILTRPGMEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSG
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAFVGFMLILV
VVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

Important features:

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 230-255

N-glycosylation sites.

amino acids 40-43 and 134-137

Tissue factor proteins homology.

amino acids 92-119

Integrins alpha chain protein homology.

amino acids 232-262

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FIGURE 118

CGGACGCGTGGGCCGCCACCTCCGGAACAAGCCATGGTGGCGGCGACGGTGGCAGCGGCGTG GCTGCTCCTGTGGGCTGCGGCCTGCGCGCAGCAGGAGCAGGACTTCTACGACTTCAAGGCGG TCAACATCCGGGGCAAACTGGTGTCGCTGGAGAAGTACCGCGGATCGGTGTCCCTGGTGGTG AATGTGGCCAGCGAGTGCGGCTTCACAGACCAGCACTACCGAGCCCTGCAGCAGCTGCAGCG AGACCTGGGCCCCACCACTTTAACGTGCTCGCCTTCCCCTGCAACCAGTTTGGCCAACAGG AGCCTGACAGCAACAAGGAGATTGAGAGCTTTGCCCGCCGCACCTACAGTGTCTCATTCCCC ATGTTTAGCAAGATTGCAGTCACCGGTACTGGTGCCCATCCTGCCTTCAAGTACCTGGCCCA GACTTCTGGGAAGGAGCCCACCTGGAACTTCTGGAAGTACCTAGTAGCCCCAGATGGAAAGG TGGTAGGGGCTTGGGACCCAACTGTGTCAGTGGAGGAGGTCAGACCCCAGATCACAGCGCTC $\tt GTGAGGAAGCTCATCCTACTGAAGCGAGAAGACTTA{\color{red}{TAA}}CCACCGCGTCTCCTCCTCCACCA$ CCTCATCCCGCCCACCTGTGTGGGGCTGACCAATGCAAACTCAAATGGTGCTTCAAAGGGAG AGACCCACTGACTCTTCCTTTACTCTTATGCCATTGGTCCCATCATTCTTGTGGGGGAA AAATTCTAGTATTTTGATTATTTGAATCTTACAGCAACAAATAGGAACTCCTGGCCAATGAG AGCTCTTGACCAGTGAATCACCAGCCGATACGAACGTCTTGCCAACAAAAATGTGTGGCAAA TAGAAGTATATCAAGCAATAATCTCCCACCCAAGGCTTCTGTAAACTGGGACCAATGATTAC CTCATAGGGCTGTTGTGAGGATTAGGATGAAATACCTGTGAAAGTGCCTAGGCAGTGCCAGC CAAATAGGAGGCATTCAATGAACATTTTTTTGCATATAAACCAAAAAATAACTTGTTATCAAT AAAAACTTGCATCCAACATGAATTTCCAGCCGATGATAATCCAGGCCAAAGGTTTAGTTGTT GTTATTTCCTCTGTATTATTTTCTTCATTACAAAAGAAATGCAAGTTCATTGTAACAATCCA AACAATACCTCACGATATAAAATAAAAATGAAAGTATCCTCCTCAAAAA

 $\label{thm:policy} {\tt MVAATVAAAWLLLWAAACAQQEQDFYDFKAVNIRGKLVSLEKYRGSVSLVVNVASECGFTDQ} $$ {\tt HYRALQQLQRDLGPHHFNVLAFPCNQFGQQEPDSNKEIESFARRTYSVSFPMFSKIAVTGTG} $$ {\tt AHPAFKYLAQTSGKEPTWNFWKYLVAPDGKVVGAWDPTVSVEEVRPQITALVRKLILLKREDL} $$ {\tt Constant of the policy of the pol$

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CGGACGCGTGGGCGGGCCGGGACGCAAAGCGAGCCATGCTCTACGTCGGGATGC TGCGCCTGGGGAGGCTGTGCGCCGGGAGCTCGGGGGTGCTGGGGGGCCCGGGCCCCTCTCT CGGAGTTGGCAGGAAGCCAGGTTGCAGGGTGTCCGCTTCCTCAGTTCCAGAGAGGTGGATCG CATGGTCTCCACGCCCATCGGAGGCCTCAGCTACGTTCAGGGGTGCACCAAAAAGCATCTTA ACAGCAAGACTGTGGGCCAGTGCCTGGAGACCACAGCACAGAGGGTCCCAGAACGAGGCC TTGGTCGTCCTCCATGAAGACGTCAGGTTGACCTTTGCCCAACTCAAGGAGGAGGTGGACAA AGCTGCTTCTGGCCTCCTGAGCATTGGCCTCTGCAAAGGTGACCGGCTGGGCATGTGGGGAC CTAACTCCTATGCATGGGTGCTCATGCAGTTGGCCACCGCCCAGGCGGGCATCATTCTGGTG TCTGTGAACCCAGCCTACCAGGCTATGGAACTGGAGTATGTCCTCAAGAAGGTGGGCTGCAA GGCCCTTGTGTTCCCCAAGCAATTCAAGACCCAGCAATACTACAACGTCCTGAAGCAGATCT GTCCAGAAGTGGAGAATGCCCAGCCAGGGGCCTTGAAGAGTCAGAGGCTCCCAGATCTGACC ACAGTCATCTCGGTGGATGCCCCTTTGCCGGGGACCCTGCTCCTGGATGAAGTGGTGGCGGC TGGCAGCACACGCAGCATCTGGACCAGCTCCAATACAACCAGCAGTTCCTGTCCTGCCATG ACCCCATCAACATCCAGTTCACCTCGGGGACAACAGGCAGCCCCAAGGGGGGCCACCCTCTCC CACTACAACATTGTCAACAACTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGAC ACCAGAGCAGTTGCGGATGATCCTGCCCAACCCCTGTACCATTGCCTGGGTTCCGTGGCAG GCACAATGATGTCTGATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGC AAGAAGGCACTGGAGGCCATCAGCAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGAT GTTCGTGGACATTCTGAACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAG GTGTCATTGCTGGGTCCCCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAAT ATGAAGGACCTGGTGGTTGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTT CCCTGAGGACACTGTGGAGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGG CCCGGATCATGAACATGGAGGCAGGGACGCTGGCAAAGCTGAACACGCCCGGGGAGCTGTGC ATCCGAGGGTACTGCGTCATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGT AGATCGTGGGCCGCTCTAAGGATATGATCATCCGGGGTGGTGAGAACATCTACCCCGCAGAG CTCGAGGACTTCTTTCACACACCCGAAGGTGCAGGAAGTGCAGGTGGTGGGAGTGAAGGA CGATCGGATGGGGAAGAGATTTGTGCCTGCATTCGGCTGAAGGACGGGGAGAGACCACGG TGGAGGAGATAAAAGCTTTCTGCAAAGGGAAGATCTCTCACTTCAAGATTCCGAAGTACATC GTGTTTGTCACAAACTACCCCCTCACCATTTCAGGAAAGATCCAGAAATTCAAACTTCGAGA GCAGATGGAACGACATCTAAATCTG**TGA**ATAAAGCAGCAGGCCTGTCCTGGCCGGTTGGCTT GACTCTCTCTGTCAGAATGCAACCTGGCTTTATGCACCTAGATGTCCCCAGCACCCAGTTC TCCATCCCCACATTCCCCTGTCTGTCCTTGTGATTTGGCATAAAGAGCTTCTGTTTTCTTT GAAAAAAAAAAAAAA

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FIGURE 122

MAVYVGMLRLGRLCAGSSGVLGARAALSRSWQEARLQGVRFLSSREVDRMVSTPIGGLSYVQ
GCTKKHLNSKTVGQCLETTAQRVPEREALVVLHEDVRLTFAQLKEEVDKAASGLLSIGLCKG
DRLGMWGPNSYAWVLMQLATAQAGIILVSVNPAYQAMELEYVLKKVGCKALVFPKQFKTQQY
YNVLKQICPEVENAQPGALKSQRLPDLTTVISVDAPLPGTLLLDEVVAAGSTRQHLDQLQYN
QQFLSCHDPINIQFTSGTTGSPKGATLSHYNIVNNSNILGERLKLHEKTPEQLRMILPNPLY
HCLGSVAGTMMCLMYGATLILASPIFNGKKALEAISRERGTFLYGTPTMFVDILNQPDFSSY
DISTMCGGVIAGSPAPPELIRAIINKINMKDLVVAYGTTENSPVTFAHFPEDTVEQKAESVG
RIMPHTEARIMNMEAGTLAKLNTPGELCIRGYCVMLGYWGEPQKTEEAVDQDKWYWTGDVAT
MNEQGFCKIVGRSKDMIIRGGENIYPAELEDFFHTHPKVQEVQVVGVKDDRMGEEICACIRL
KDGEETTVEEIKAFCKGKISHFKIPKYIVFVTNYPLTISGKIQKFKLREQMERHLNL

FIGURE 124

GAGCAGGACGGAGCCATGGACCCCGCCAGGAAAGCAGGTGCCCAGGCCATGATCTGGACTGC AGGCTGGCTGCTGCTGCTGCTTCGCGGAGGAGCGCAGGCCCTGGAGTGCTACAGCTGCG TGCAGAAAGCAGATGACGGATGCTCCCCGAACAAGATGAAGACAGTGAAGTGCGCGCCGGGC GTGGACGTCTGCACCGAGGCCGTGGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGC AGTGCGGGGTTGCGGTTCGGGACTCCCCGGCAAGAATGACCGCGGCCTGGATCTTCACGGGC TTCTGGCGTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAAGCTCAACCTC ACCTCGCGGCGCTCGACCCGGCAGGTAATGAGAGTGCATACCCGCCCAACGGCGTGGAGTG CTACAGCTGTGTGGGCCTGAGCCGGGAGGCGTGCCAGGGTACATCGCCGCCGGTCGTGAGCT GCTACAACGCCAGCGATCATGTCTACAAGGGCTGCTTCGACGGCAACGTCACCTTGACGGCA GCTAATGTGACTGTGTCCTTGCCTGTCCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGA TGGAGTAACAGGCCCAGGGTTCACGCTCAGTGGCTCCTGTTGCCAGGGGTCCCGCTGTAACT CTGACCTCCGCAACAAGACCTACTTCTCCCCTCGAATCCCACCCCTTGTCCGGCTGCCCCCT CCAGAGCCCACGACTGTGGCCTCAACCACATCTGTCACCACTTCTACCTCGGCCCCAGTGAG ACCCACATCCACCACCAAACCCATGCCAGCGCCAACCAGTCAGACTCCGAGACAGGGAGTAG AACACGAGGCCTCCCGGGATGAGGAGCCCAGGTTGACTGGAGGCGCCGCTGGCCACCAGGAC CGCAGCAATTCAGGGCAGTATCCTGCAAAAGGGGGGCCCCAGCAGCCCCCATAATAAAGGCTG TGTGGCTCCCACAGCTGGATTGGCAGCCCTTCTGTTGGCCGTGGCTGCTGGTGTCCTACTGT GAGCTTCTCCACCTGGAAATTTCCCTCTCACCTACTTCTCTGGCCCTGGGTACCCCTCTTCT CATCACTTCCTGTTCCCACCACTGGACTGGGCTGGCCCAGCCCCTGTTTTTCCAACATTCCC CAGTATCCCCAGCTTCTGCTGCGCTGGTTTGCGGCTTTGGGAAATAAAATACCGTTGTATAT ATTCTGCCAGGGGTGTTCTAGCTTTTTGAGGACAGCTCCTGTATCCTTCTCATCCTTGTCTC TCCGCTTGTCCTCTTGTGATGTTAGGACAGAGTGAGAAGTCAGCTGTCACGGGGAAGGTG GGTGGGTGGGACAATGGCTCCCCACTCTAAGCACTGCCTCCCCTACTCCCCGCATCTTTGGG GAATCGGTTCCCCATATGTCTTCCTTACTAGACTGTGAGCTCCTCGAGGGGGGGCCCGGTAC CCAATTCGCCCTATAGTGAGTCGTA

MDPARKAGAQAMIWTAGWLLLLLRGGAQALECYSCVQKADDGCSPNKMKTVKCAPGVDVCT
EAVGAVETIHGQFSLAVRGCGSGLPGKNDRGLDLHGLLAFIQLQQCAQDRCNAKLNLTSRAL
DPAGNESAYPPNGVECYSCVGLSREACQGTSPPVVSCYNASDHVYKGCFDGNVTLTAANVTV
SLPVRGCVQDEFCTRDGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPRIPPLVRLPPPEPTT
VASTTSVTTSTSAPVRPTSTTKPMPAPTSQTPRQGVEHEASRDEEPRLTGGAAGHQDRSNSG
QYPAKGGPQQPHNKGCVAPTAGLAALLLAVAAGVLL

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FIGURE 126

CGGGACTCGGCGGTCCTCCTGGGAGTCTCGGAGGGGACCGGCTGTGCAGACGCCATGGAGT TGGTGCTGGTCTTCCTCTGCAGCCTGCTGGCCCCCATGGTCCTGGCCAGTGCAGCTGAAAAG GAGAAGGAAATGGACCCTTTTCATTATGATTACCAGACCCTGAGGATTGGGGGACTGGTGTT CGCTGTGGTCCTCTTCTCGGTTGGGATCCTCCTTATCCTAAGTCGCAGGTGCAAGTGCAGTT TCAATCAGAAGCCCCGGGCCCCAGGAGATGAGGAAGCCCAGGTGGAGAACCTCATCACCGCC AATGCAACAGAGCCCCAGAAGCAGAGAACTGAAGTGCAGCCATCAGGTGGAAGCCTCTGGAA ${\tt CCTGAGGCGGCTGCTTGAACCTTTGGATGCAAATGTCGATGCT} {\color{red}{\textbf{TAA}}} {\color{red}{\textbf{GAAAACCGGCCACTTC}}}$ AGCAACAGCCCTTTCCCCAGGAGAAGCCAAGAACTTGTGTGTCCCCCACCCTATCCCCTCTA ACACCATTCCTCCACCTGATGATGCAACTAACACTTGCCTCCCCACTGCAGCCTGCGGTCCT CCCAGGCAGGGGCTGAGCCACATGGCCATCTGCTCCTCCCTGCCCCCGTGGCCCTCCATCAC CTTCTGCTCCTAGGAGGCTGCTTGTTGCCCGAGACCAGCCCCCTCCCCTGATTTAGGGATGC GTAGGGTAAGAGCACGGGCAGTGGTCTTCAGTCGTCTTGGGACCTGGGAAGGTTTGCAGCAC TTTGTCATCATCTTCATGGACTCCTTTCACTCCTTTAACAAAAACCTTGCTTCCTTATCCC ACCTGATCCCAGTCTGAAGGTCTCTTAGCAACTGGAGATACAAAGCAAGGAGCTGGTGAGCC CAGCGTTGACGTCAGGCAGGCTATGCCCTTCCGTGGTTAATTTCTTCCCAGGGGCTTCCACG AGGAGTCCCCATCTGCCCCGCCCCTTCACAGAGCGCCCGGGGATTCCAGGCCCAGGGCTTCT ACTCTGCCCCTGGGAATGTGTCCCCTGCATATCTTCTCAGCAATAACTCCATGGGCTCTGG GACCCTACCCCTTCCAACCTTCCCTGCTTCTGAGACTTCAATCTACAGCCCAGCTCATCCAG GTTGGGGCCAGCACCCGGGATGGATGGAGGGGAGAGCAGAGGCCTTTGCTTCTCTGCCTACG TCCCCTTAGATGGGCAGCAGAGGCAACTCCCGCATCCTTTGCTCTGCCTGTCGGTGGTCAGA GCGGTGAGCGAGGTTGGAGACTCAGCAGGCTCCGTGCAGCCCTTGGGAACAGTGAGAG GTTGAAGGTCATAACGAGAGTGGGAACTCAACCCAGATCCCGCCCCTCCTGTCCTCTGTGTT CCCGCGGAAACCAACCGTGCGCTGTGACCCATTGCTGTTCTCTGTATCGTGATCTAT CCTCAACAACAACAGAAAAAAGGAATAAAATATCCTTTGTTTCCT

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHYDYQTLRIGGLVFAVVLFSVGILLILSRRCK CSFNQKPRAPGDEEAQVENLITANATEPQKQRTEVQPSGGSLWNLRRLLEPLDANVDA

_131/310 FIGURE 128

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 ${\tt MKIPVLPAVVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSAFKADE}$ ${\tt FLNWHALFESIKRKLPFLNWDAFPKLKGLRSATPDAQ}$

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FIGURE 131

 ${\tt MGVEIAFASVILTCLSLLAAGVSQVVLLQPVPTQETGPKAMGDLSCGFAGHS}$

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FIGURE 132

GGGGAATCTGCAGTAGGTCTGCCGGCGATGGAGTGGTGGGCTAGCTCGCCGCTTCGGCTCTG GCTGCTGTTGTTCCTCCTGCCCTCAGCGCCAGGGCCGCCAGAAGGAGTCAGGTTCAAAATGGA AAGTATTTATTGACCAAATTAACAGGTCTTTGGAGAATTACGAACCATGTTCAAGTCAAAAC TGCAGCTGCTACCATGGTGTCATAGAAGAGGATCTAACTCCTTTCCGAGGAGGCATCTCCAG GAAGATGATGGCAGAGGTAGTCAGACGGAAGCTAGGGACCCACTATCAGATCACTAAGAACA GACTGTACCGGGAAAATGACTGCATGTTCCCCTCAAGGTGTAGTGGTGTTGAGCACTTTATT TTGGAAGTGATCGGGCGTCTCCCTGACATGGAGATGGTGATCAATGTACGAGATTATCCTCA GGTTCCTAAATGGATGGAGCCTGCCATCCCAGTCTTCTCCTTCAGTAAGACATCAGAGTACC ATGATATCATGTATCCTGCTTGGACATTTTGGGAAGGGGGACCTGCTGTTTGGCCAATTTAT CCTACAGGTCTTGGACGTGGGACCTCTTCAGAGAAGATCTGGTAAGGTCAGCAGCACAGTG GCCATGGAAAAAGAAAAACTCTACAGCATATTTCCGAGGATCAAGGACAAGTCCAGAACGAG ATCCTCTCATTCTTCTGTCTCGGAAAAACCCAAAACTTGTTGATGCAGAATACACCAAAAAC CAGGCCTGGAAATCTATGAAAGATACCTTAGGAAAGCCAGCTGCTAAGGATGTCCATCTTGT GGATCACTGCAAATACAAGTATCTGTTTAATTTTCGAGGCGTAGCTGCAAGTTTCCGGTTTA AACACCTCTTCCTGTGTGGCTCACTTGTTTTCCATGTTGGTGATGAGTGGCTAGAATTCTTC TATCCACAGCTGAAGCCATGGGTTCACTATATCCCAGTCAAAACAGATCTCTCCAATGTCCA AGAGCTGTTACAATTTGTAAAAGCAAATGATGATGTAGCTCAAGAGATTGCTGAAAGGGGAA GCCAGTTTATTAGGAACCATTTGCAGATGGATGACATCACCTGTTACTGGGAGAACCTCTTG AGTGAATACTCTAAATTCCTGTCTTATAATGTAACGAGAAGGAAAGGTTATGATCAAATTAT TCCCAAAATGTTGAAAACTGAACTATAGTAGTCATCATAGGACCATAGTCCTCTTTGTGGCA ACAGATCTCAGATATCCTACGGTGAGAAGCTTACCATAAGCTTGGCTCCTATACCTTGAATA TCTGCTATCAAGCCAAATACCTGGTTTTCCTTATCATGCTGCACCCAGAGCAACTCTTGAGA AAGATTTAAAATGTGTCTAATACACTGATATGAAGCAGTTCAACTTTTTGGATGAATAAGGA CCAGAAATCGTGAGATGTGGATTTTGAACCCAACTCTACCTTTCATTTTCTTAAGACCAATC ACAGCTTGTGCCTCAGATCATCCACCTGTGTGAGTCCATCACTGTGAAATTGACTGTGTCCA TGTGATGATGCCCTTTGTCCCATTATTTGGAGCAGAAAATTCGTCATTTGGAAGTAGTACAA CTCATTGCTGGAATTGTGAAATTATTCAAGGCGTGATCTCTGTCACTTTATTTTAATGTAGG AAACCCTATGGGGTTTATGAAAAATACTTGGGGATCATTCTCTGAATGGTCTAAGGAAGCGG TAGCCATGCCATGCAATGATGTAGGAGTTCTCTTTTGTAAAACCATAAACTCTGTTACTCAG GAGGTTTCTATAATGCCACATAGAAAGAGGCCAATTGCATGAGTAATTATTGCAATTGGATT TCAGGTTCCCTTTTTGTGCCTTCATGCCCTACTTCTTAATGCCTCTCTAAAGCCAAA

MEWWASSPLRLWLLLFLLPSAQGRQKESGSKWKVFIDQINRSLENYEPCSSQNCSCYHGVIE EDLTPFRGGISRKMMAEVVRRKLGTHYQITKNRLYRENDCMFPSRCSGVEHFILEVIGRLPD MEMVINVRDYPQVPKWMEPAIPVFSFSKTSEYHDIMYPAWTFWEGGPAVWPIYPTGLGRWDL FREDLVRSAAQWPWKKKNSTAYFRGSRTSPERDPLILLSRKNPKLVDAEYTKNQAWKSMKDT LGKPAAKDVHLVDHCKYKYLFNFRGVAASFRFKHLFLCGSLVFHVGDEWLEFFYPQLKPWVH YIPVKTDLSNVQELLQFVKANDDVAQEIAERGSQFIRNHLQMDDITCYWENLLSEYSKFLSY NVTRRKGYDQIIPKMLKTEL

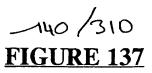
FIGURE 134

 ${\tt CACCCCTCCATTTCTCGCC} {\tt ATG} {\tt GCCCCTGCACTGCTCCTGATCCCTGCTCCCTCTCTT}$ TCATCCTGGCCTTTGGCACCGGAGTGGAGTTCGTGCGCTTTACCTCCCTTCGGCCACTTCTT CCGCAGCATCCTTGCCCCCCTGGCATGGGATCTGGGGCTCCTGCTTCTATTTGTTGGGCAGC ACAGCCTCATGGCAGCTGAAAGAGTGAAGGCATGGACATCCCGGTACTTTGGGGTCCTTCAG AGGTCACTGTATGTGGCCTGCACTGCCCTTGCAGCTGGTGATGCGGTACTGGGAGCC CATACCCAAAGGCCCTGTGTTGTGGGAGGCTCGGGCTGAGCCATGGGCCACCTGGGTGCCGC TCCTCTGCTTTGTGCTCCATGTCATCTCCTGGCTCCTCATCTTTAGCATCCTTCTCGTCTTT GACTATGCTGAGCTCATGGGCCTCAAACAGGTATACTACCATGTGCTGGGGCTGGGCGAGCC TCTGGCCCTGAAGTCTCCCCGGGCTCTCAGACTCTTCTCCCACCTGCGCCACCCAGTGTGTG TGGAGCTGCTGACAGTGCTGTGGGTGGTGCCTACCCTGGGCACGGACCGTCTCCTTGCT TTCCTCCTTACCCTCTGGGCCTGGCTCACGGGCTTGATCAGCAAGACCTCCGCTACCT ${\tt CCGGGCCCAGCTACAAAGAAAACTCCACCTGCTCTCTCGGCCCCAGGATGGGGAGGCAGAG{f T}}$ GAGGAGCTCACTCTGGTTACAAGCCCTGTTCTTCCTCTCCCACTGAATTCTAAATCCTTAAC ATCCAGGCCCTGGCTGCTTCATGCCAGAGGCCCAAATCCATGGACTGAAGGAGATGCCCCTT CTACTACTTGAGACTTTATTCTCTGGGTCCAGCTCCATACCCTAAATTCTGAGTTTCAGCCA CTGAACTCCAAGGTCCACTTCTCACCAGCAAGGAAGAGTGGGGTATGGAAGTCATCTGTCCC TTCACTGTTTAGAGCATGACACTCTCCCCCTCAACAGCCTCCTGAGAAGGAAAGGATCTGCC CTGACCACTCCCCTGGCACTGTTACTTGCCTCTGCGCCTCAGGGGTCCCCTTCTGCACCGCT GGCTTCCACTCCAAGAAGGTGGACCAGGGTCTGCAAGTTCAACGGTCATAGCTGTCCCTCCA GGCCCCAACCTTGCCTCACCACTCCCGGCCCTAGTCTCTGCACCTCCTTAGGCCCTGCTCT GGGCTCAGACCCAACCTAGTCAAGGGGATTCTCCTGCTCTTAACTCGATGACTTGGGGCTC

-138/310 FIGURE 135

MAPALLLIPAALASFILAFGTGVEFVRFTSLRPLLGGIPESGGPDARQGWLAALQDRSILAP LAWDLGLLLLFVGQHSLMAAERVKAWTSRYFGVLQRSLYVACTALALQLVMRYWEPIPKGPV LWEARAEPWATWVPLLCFVLHVISWLLIFSILLVFDYAELMGLKQVYYHVLGLGEPLALKSP RALRLFSHLRHPVCVELLTVLWVVPTLGTDRLLLAFLLTLYLGLAHGLDQQDLRYLRAQLQR KLHLLSRPQDGEAE

CCGAGCACAGGAGATTGCCTGCGTTTAGGAGGTGGCTGCGTTGTGGGAAAAGCTATCAAGGA AGAAATTGCCAAACCATGTCTTTTTTCTGTTTTCAGAGTAGTTCACAACAGATCTGAGTGT TTTAATTAAGCATGGAATACAGAAAACAACAAAAAACTTAAGCTTTAATTTCATCTGGAATT TCACGTGGTGCTCTCCGACTACTCACCCCGAGTGTAAAGAACCTTCGGCTCGCGTGCTTCTG ${\tt AGCTGCTGTGG} \underline{\textbf{ATG}} \texttt{GCCTCGGCTCTCTGGACTGTCCTTCCGAGTAGGATGTCACTGAGATCC}$ CTCAAATGGAGCCTCCTGCTGCTGTCACTCCTGAGTTTCTTTGTGATGTGGTACCTCAGCCT TCCCCACTACAATGTGATAGAACGCGTGAACTGGATGTACTTCTATGAGTATGAGCCGATTT ACAGACAAGACTTTCACTTCACACTTCGAGAGCATTCAAAACTGCTCTCATCAAAATCCATTT TTGGGGTGAAAAAAGTCTTGGTGGGGATATGAGGTTCTTACATTTTTCTTATTAGGCCAAG AGGCTGAAAAGGAAGACAAAATGTTGGCATTGTCCTTAGAGGATGAACACCTTCTTTATGGT GACATAATCCGACAAGATTTTTTAGACACATATAATAACCTGACCTTGAAAACCATTATGGC TTTTCATCAATACTGGCAATTTAGTGAAGTATCTTTTAAACCTAAACCACTCAGAGAAGTTT TTCACAGGTTATCCTCTAATTGATAATTATTCCTATAGAGGATTTTACCAAAAAACCCATAT TTCTTACCAGGAGTATCCTTTCAAGGTGTTCCCTCCATACTGCAGTGGGTTGGGTTATATAA TGTCCAGAGATTTGGTGCCAAGGATCTATGAAATGATGGGTCACGTAAAACCCATCAAGTTT GAAGATGTTTATGTCGGGATCTGTTTGAATTTATTAAAAGTGAACATTCATATTCCAGAAGA CAGCCCATGGCTTTTCTTCCAAGGAGATCATCACTTTTTGGCAGGTCATGCTAAGGAACACC ACATGCCATTAT<u>TAA</u>CTTCACATTCTACAAAAAGCCTAGAAGGACAGGATACCTTGTGGAAA GTGTTAAATAAAGTAGGTACTGTGGAAAATTCATGGGGAGGTCAGTGTGCTGGCTTACACTG AACTGAAACTCATGAAAAACCCAGACTGGAGACTGGAGGGTTACACTTGTGATTTATTAGTC AGGCCCTTCAAAGATGATATGTGGAGGAATTAAATATAAAGGAATTGGAGGTTTTTGCTAAA GAAATTAATAGGACCAAACAATTTGGACATGTCATTCTGTAGACTAGAATTTCTTAAAAGGG AACAATGTAGTCACTTGAAGGTTTTGTGTATATCTTATGTGGATTACCAATTTAAAAATATA TGTAGTTCTGTGTCAAAAAACTTCTTCACTGAAGTTATACTGAACAAAATTTTACCTGTTTT CTTCAACTTTGTGTTTTTAAATGTTTTGACGATTTCAATACAAGATAAAAAGGATAGTGAAT CATTCTTTACATGCAAACATTTTCCAGTTACTTAACTGATCAGTTTATTATTGATACATCAC TCCATTAATGTAAAGTCATAGGTCATTATTGCATATCAGTAATCTCTTGGACTTTGTTAAAT ATTTTACTGTGGTAATATAGAGAAGAATTAAAGCAAGAAAATCTGAAAA



MASALWTVLPSRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNWMYFYEYEPIYRQD FHFTLREHSNCSHQNPFLVILVTSHPSDVKARQAIRVTWGEKKSWWGYEVLTFFLLGQEAEK EDKMLALSLEDEHLLYGDIIRQDFLDTYNNLTLKTIMAFRWVTEFCPNAKYVMKTDTDVFIN TGNLVKYLLNLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQEYPFKVFPPYCSGLGYIMSRD LVPRIYEMMGHVKPIKFEDVYVGICLNLLKVNIHIPEDTNLFFLYRIHLDVCQLRRVIAAHG FSSKEIITFWQVMLRNTTCHY

______/310 FIGURE 138

MKFTIVFAGLLGVFLAPALANYNINVNDDNNNAGSGQQSVSVNNEHNVANVDNNNGWDSWNS IWDYGNGFAATRLFQKKTCIVHKMNKEVMPSIQSLDALVKEKKLQGKGPGGPPPKGLMYSVN PNKVDDLSKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

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FIGURE 140

CATTTCTGAAACTAATCGTGTCAGAATTGACTTTGAAAAGCATTGCTTTTTACAGAAGTATA TTAACTTTTTAGGAGTAATTTCTAGTTTGGATTGTAATATGAAATAATTTAAAAGGGCTTCG CTCATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTCTTATTGCTTACTGATTTTTT TTGTTCGATTTCAACCAGAGACTATAGCATGTGCTTGCATCTACCTTGCAGCTAGAGCACTT CAGATTCCGTTGCCAACTCGTCCCCATTGGTTTCTTCTTTTTGGTACTACAGAAGAGGGAAAT CCAGGAAATCTGCATAGAAACACTTAGGCTTTATACCAGAAAAAAGCCAAACTATGAATTAC TGGAAAAAGAAGTAGAAAAAAGAAAAGTAGCCTTACAAGAAGCCAAATTAAAAGCAAAGGGA TTGAATCCGGATGGAACTCCAGCCCTTTCAACCCTGGGTGGATTTTCTCCAGCCTCCAAGCC ATCATCACCAAGAGAAGTAAAAGCTGAAGAGAAATCACCAATCTCCATTAATGTGAAGACAG TCAAAAAGAACCTGAGGATAGACAACAGGCTTCCAAAAGCCCTTACAATGGTGTAAGAAAA TTCTAGATCACATACTCCAAGAAGACACTATAATAATAGGCGGAGTCGATCTGGAACATACA GCTCGAGATCAAGAAGCAGGTCCCGCAGTCACAGTGAAAGCCCTCGAAGACATCATAATCAT GGTTCTCCTCACCTTAAGGCCAAGCATACCAGAGATGATTTAAAAAGTTCAAACAGACATGG TCATAAAAGGAAAAAATCTCGTTCTCGATCTCAGAGCAAGTCTCGGGATCACTCAGATGCAG CCAAGAACACAGGCATGAAAGGGGACATCATAGGGACAGGCGTGAACGATCTCGCTCCTTT CTGACTTTCTCTTCCTTTGAGCCTGCATCAGTTCTTGGTTTTTGCCTATCTACAGTGTGATGT ATGGACTCAATCAAAAACATTAAACGCAAACTGATTAGGATTTGATTCTTGAAACCCTCTA AAAATGCCCTAGCAGTATCTAATTAAAAACCATGGTCAGGTTCAATTGTACTTTATTATAGT TGTGTATTGTTTATTGCTATAAGAACTGGAGCGTGAATTCTGTAAAAATGTATCTTATTTTT ATACAGATAAAATTGCAGACACTGTTCTATTTAAGTGGTTATTTGTTTAAATGATGGTGAAT ACTTTCTTAACACTGGTTTGTCTGCATGTGTAAAGATTTTTACAAGGAAATAAAATACAAAT CTTGTTTTTCTAAAAAAAAAAAAAAAAAAAGT

MNDSLRTNVFVRFQPETIACACIYLAARALQIPLPTRPHWFLLFGTTEEEIQEICIETLRLY
TRKKPNYELLEKEVEKRKVALQEAKLKAKGLNPDGTPALSTLGGFSPASKPSSPREVKAEEK
SPISINVKTVKKEPEDRQQASKSPYNGVRKDSKRSRNSRSASRSRSRTRSRSRSHTPRRHYN
NRRSRSGTYSSRSRSRSRSHSESPRRHHNHGSPHLKAKHTRDDLKSSNRHGHKRKKSRSRSQ
SKSRDHSDAAKKHRHERGHHRDRRERSRSFERSHKSKHHGGSRSGHGRHRR

_146/340 FIGURE 143

GGCACGAGGCCTCGTGCCAAGCTTGGCACGAGGGTGCACCGCGTTCTCGCACGCGTCATGGC GGTCCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCACCCTCATGCACAGGCTGGCGC CACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGCAGTTTGTTCCGATACAAGCACCCG TCTGAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCCCAGAGGCAGGAAAGAGCGGTG GGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCCGAGATGCCCCGTTCCAGCTGG AGACCTGCCCCTCACGACCGTGGATGCCCTGGTCCTGCGCTTCTTCCTGGAGTACCAGTGG TTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGTACCTCTTCACAGAGGCCTACTACTACAT GCTGGGACCAGCCAAGGAGACTAACATTGCTGTTCTGGTGCCTGCTCACGGTGACCTTCT CCATCAAGATGTTCCTGACAGTGACACGGCTGTACTTCAGCGCCGAGGAGGGGGGGTGAGCGC TCTGTCTGCCTCACCTTTGCCTTCCTCTCTGCTGCTGGCCATGCTGGTGCAAGTGGTGCG GGAGGAGACCCTCGAGCTGGGCCTGGAGCCTGGTCTGGCCAGCATGACCCAGAACTTAGAGC CACTTCTGAAGAAGCAGGCTGGGACTGGGCGCTTCCTGTGGCCAAGCTGGCTATCCGCGTG GGACTGGCAGTGGGGCTCTGTGCTGGGTGCCTTCCTCACCTTCCCAGGCCTGCGGCTGGC CCAGACCCACCGGGACGCACTGACCATGTCGGAGGACAGACCCATGCTGCAGTTCCTCCTGC ACACCAGCTTCCTGTCTCCCCTGTTCATCCTGTGGCTCTGGACAAAGCCCATTGCACGGGAC TTCCTGCACCAGCCGCCGTTTGGGGAGACGCGTTTCTCCCTGCTGTCCGATTCTGCCTTCGA CTCTGGGCGCCTCTGGTTGCTGGTGGTGCTGCTGCGGGTGGCGGTGACCCGGCCCC ACCTGCAGGCCTACCTGTGCCTGGCCAAGGCCCGGGTGGAGCAGCTGCGAAGGGAGGCTGGC CGCATCGAAGCCCGTGAAATCCAGCAGAGGGTGGTCCGAGTCTACTGCTATGTGACCGTGGT GAGCTTGCAGTACCTGACGCCGCTCATCCTCACCTCAACTGCACACTTCTGCTCAAGACGC TGGGAGGCTATTCCTGGGGCCTGGGCCCAGCTCCTCTACTATCCCCCGACCCATCCTCAGCC AGCGCTGCCCCCATCGGCTCTGGGGAGGACGAAGTCCAGCAGACTGCAGCGCGGATTGCCGG GGCCCTGGGTGGCCTTACTCCCCTCTTCCTCCGTGGCGTCCTGGCCTACCTCATCTGGT GGACGGCTGCCTGCCAGCTCTCGCCAGCCTTTTCGGCCTCTACTTCCACCAGCACTTGGCA GGCTCCTAGCTGCCTGCAGACCCTCCTGGGGCCCTGAGGTCTGTTCCTGGGGCAGCGGGACA CTAGCCTGCCCCTCTGTTTGCGCCCCCGTGTCCCCAGCTGCAAGGTGGGGCCGGACTCCCC GGCGTTCCCTTCACCACAGTGCCTGACCCGCGGCCCCCTTGGACGCCGAGTTTCTGCCTCA GAACTGTCTCTCCTGGGCCCAGCAGCATGAGGGTCCCGAGGCCATTGTCTCCGAAGCGTATG TGCCAGGTTTGAGTGGCGAGGGTGATGCTGGCTGCTCTTCTGAACAAATAAAGGAGCATGCC GATTTTTAA

MAVLGVQLVVTLLTATLMHRLAPHCSFARWLLCNGSLFRYKHPSEEELRALAGKPRPRGRKE
RWANGLSEEKPLSVPRDAPFQLETCPLTTVDALVLRFFLEYQWFVDFAVYSGGVYLFTEAYY
YMLGPAKETNIAVFWCLLTVTFSIKMFLTVTRLYFSAEEGGERSVCLTFAFLFLLLAMLVQV
VREETLELGLEPGLASMTQNLEPLLKKQGWDWALPVAKLAIRVGLAVVGSVLGAFLTFPGLR
LAQTHRDALTMSEDRPMLQFLLHTSFLSPLFILWLWTKPIARDFLHQPPFGETRFSLLSDSA
FDSGRLWLLVVLCLLRLAVTRPHLQAYLCLAKARVEQLRREAGRIEAREIQQRVVRVYCYVT
VVSLQYLTPLILTLNCTLLLKTLGGYSWGLGPAPLLSPDPSSASAAPIGSGEDEVQQTAARI
AGALGGLLTPLFLRGVLAYLIWWTAACQLLASLFGLYFHQHLAGS

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FIGURE 145

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FIGURE 146

GGTTCCTACATCCTCTCATCTGAGAATCAGAGAGCATAATCTTCTTACGGGCCCGTGATTTA TTAACGTGGCTTAATCTGAAGGTTCTCAGTCAAATTCTTTGTGATCTACTGATTGTGGGGGC ATGGCAAGGTTTGCTTAAAGGAGCTTGGCTGGTTTGGGCCCTTGTAGCTGACAGAAGGTGGC CAGGGAGAATGCAGCACACTGCTCGGAGAATGAAGGCGCTTCTGTTGCTTGGCCTTGG CTCAGTCCTGCTAACTACATTGACAATGTGGGCAACCTGCACTTCCTGTATTCAGAACTCTG TAAAGGTGCCTCCCACTACGGCCTGACCAAAGATAGGAAGAGGCGCTCACAAGATGGCTGTC CAGACGGCTGTGCGAGCCTCACAGCCACGGCTCCCCCCAGAGGTTTCTGCAGCTGCCACC ATCTCCTTAATGACAGACGAGCCTGGCCTAGACAACCCTGCCTACGTGTCCTCGGCAGAGGA CGGGCAGCCAGCAATCAGCCCAGTGGACTCTGGCCGGAGCAACCGAACTAGGGCACGGCCCT CGAAGGACAAAGAGCGGGAGTGCAGTTGCCAACCATGCCGACCAGGGCAGGGAAAATTCTGA AAACACCACTGCCCCTGAAGTCTTTCCAAGGTTGTACCACCTGATTCCAGATGGTGAAATTA CCAGCATCAAGATCAATCGAGTAGATCCCAGTGAAAGCCTCTCTATTAGGCTGGTGGGAGGT AGCGAAACCCCACTGGTCCATATCATTATCCAACACATTTATCGTGATGGGGTGATCGCCAG AGACGGCCGGCTACTGCCAGGAGACATCATTCTAAAGGTCAACGGGATGGACATCAGCAATG TCCCTCACAACTACGCTGTGCGTCTCCTGCGGCAGCCCTGCCAGGTGCTGTGGCTGACTGTG ATGCGTGAACAGAAGTTCCGCAGCAGGAACAATGGACAGGCCCCGGATGCCTACAGACCCCG AGATGACAGCTTTCATGTGATTCTCAACAAAAGTAGCCCCGAGGAGCAGCTTGGAATAAAAC TGGTGCGCAAGGTGGATGAGCCTGGGGTTTTCATCTTCAATGTGCTGGATGGCGGTGTGGCA TATCGACATGGTCAGCTTGAGGAGAATGACCGTGTGTTAGCCATCAATGGACATGATCTTCG ATATGCAGCCCAGAAAGTGCGGCTCATCTGATTCAGGCCAGTGAAAGACGTGTTCACCTCG TCGTGTCCCGCCAGGTTCGGCAGCGGAGCCCTGACATCTTTCAGGAAGCCGGCTGGAACAGC AATGGCAGCTGGTCCCCAGGGCCAGGGGAGAGAGCACCACCCCAAGCCCCTCCATCCTAC AATTACTTGTCATGAGAAGGTGGTAAATATCCAAAAAGACCCCGGTGAATCTCTCGGCATGA CCCGGAGGAGTCATAAGCAGAGATGGAAGAATAAAAACAGGTGACATTTTGTTGAATGTGGA TGGGGTCGAACTGACAGAGGTCAGCCGGAGTGAGGCAGTGGCATTATTGAAAAGAACATCAT CCTCGATAGTACTCAAAGCTTTGGAAGTCAAAGAGTATGAGCCCCAGGAAGACTGCAGCAGC CATGTGGCTGGAATTACCACGGTGCTTGTATAACTGTAAAGATATTGTATTACGAAGAAACA TTTTTCATCAAATCCATTGTTGAAGGAACACCAGCATACAATGATGGAAGAATTAGATGTGG GACTGCTGAAAGAACTTAAAGGAAGAATTACTCTAACTATTGTTTCTTGGCCTGGCACTTTT TTA**TAG**AATCAATGATGGGTCAGAGGAAAACAGAAAAATCACAAATAGGCTAAGAAGTTGAA AAAAGTATGATCATCTAATGAAAGCCAGTTACACCTCAGAAAATATGATTCCAAAAAAATTA AAACTACTAGTTTTTTTCAGTGTGGAGGATTTCTCATTACTCTACAACATTGTTTATATTT CAAGCTGATTTAAAATTTAAAATTTGGTATATGCTGAAGTCTGCCAAGGGTACATTATGGCCA TTTTTAATTTACAGCTAAAATATTTTTTAAAATGCATTGCTGAGAAACGTTGCTTTCATCAA ACAAGAATAAATATTTTTCAGAAGTTAAA

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGCPDGCASLTAT

APSPEVSAAATISLMTDEPGLDNPAYVSSAEDGQPAISPVDSGRSNRTRARPFERSTIRSRS

FKKINRALSVLRRTKSGSAVANHADQGRENSENTTAPEVFPRLYHLIPDGEITSIKINRVDP

SESLSIRLVGGSETPLVHIIIQHIYRDGVIARDGRLLPGDIILKVNGMDISNVPHNYAVRLL

RQPCQVLWLTVMREQKFRSRNNGQAPDAYRPRDDSFHVILNKSSPEEQLGIKLVRKVDEPGV

FIFNVLDGGVAYRHGQLEENDRVLAINGHDLRYGSPESAAHLIQASERRVHLVVSRQVRQRS

PDIFQEAGWNSNGSWSPGPGERSNTPKPLHPTITCHEKVVNIQKDPGESLGMTVAGGASHRE

WDLPIYVISVEPGGVISRDGRIKTGDILLNVDGVELTEVSRSEAVALLKRTSSSIVLKALEV

KEYEPQEDCSSPAALDSNHNMAPPSDWSPSWVMWLELPRCLYNCKDIVLRRNTAGSLGFCIV

GGYEEYNGNKPFFIKSIVEGTPAYNDGRIRCGDILLAVNGRSTSGMIHACLARLLKELKGRI

TLTIVSWPGTFL

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FIGURE 149

MKILVAFLVVLTIFGIQSHGYEVFNIISPSNNGGNVQETVTIDNEKNTAIVNIHAGSCSSTT IFDYKHGYIASRVLSRRACFILKMDHQNIPPLNNLQWYIYEKQALDNMFSNKYTWVKYNPLE SLIKDVDWFLLGSPIEKLCKHIPLYKGEVVENTHNVGAGGCAKAGLLGILGISICADIHV

FIGURE 150

GGCACGAGCCAGGAACTAGGAGGTTCTCACTGCCCGAGCAGAGGCCCTACACCCCACCGAGGC **ATG**GGGCTCCCTGGGCTGTTCTGCTTGGCCGTGCTGCCAGCAGCTTCTCCAAGGCACG GGAGGAAGAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCCTGGAAGTTTTCCCCAAAG GCCGCTGGGTGCTCATAACCTGCTGTGCACCCCAGCCACCACCGCCCATCACCTATTCCCTC TGTGGAACCAAGAACATCAAGGTGGCCAAGAAGGTGGTGAAGACCCACGAGCCGGCCTCCTT CAACCTCAACGTCACACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCCT CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG CCAGTGTCTGAGCTGCGGGCCAACTTCACTCTGCAGGACAGAGGGGCAGGCCCCAGGGTGGA GATGATCTGCCAGGCGTCCTCGGGCAGCCCACCTATCACCAACAGCCTGATCGGGAAGGATG AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAACGCCAATGTCCAGCACAGCGC CCTCACAGTGGTGCCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCCTGGAGA GCCCCATCCTTGCCTTGCCGCTCTACAGGAGCACCCGCCGTCTGAGTGAAGAGGAGTTTGGG GGGTTCAGGATAGGGAATGGGGAGGTCAGAGGACGCAAAGCAGCAGCCATG<u>TAG</u>AATGAACC GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCACTGTTCGTATTTGGA

FIGURE 151

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVFPKGRWVLITCCAPQPPPPITYSL CGTKNIKVAKKVVKTHEPASFNLNVTLKSSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK PVSELRANFTLQDRGAGPRVEMICQASSGSPPITNSLIGKDGQVHLQQRPCHRQPANFSFLP SQTSDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPILALPLYRSTRRLSEEEFG GFRIGNGEVRGRKAAAM

155/310 FIGURE 152

 ${\tt GGTCCTTA} \underline{\textbf{ATG}} {\tt GCAGCAGCCGCCGCTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTG}$ CTGTCCGGCTGGTCCCGGGCTGGGCGAGCCGACCCTCACTCTCTTTGCTATGACATCACCGT CATCCCTAAGTTCAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGA CTTTTCTTCACTATGACTGTGGCAACAAGACAGTCACACCTGTCAGTCCCCTGGGGAAGAAA CTAAATGTCACAACGGCCTGGAAAGCACAGAACCCAGTACTGAGAGAGGTGGTGGACATACT TACAGAGCAACTGCGTGACATTCAGCTGGAGAATTACACACCCAAGGAACCCCTCACCCTGC AGGCAAGGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTTGGCAGTTCAGT TTCGATGGGCAGATCTTCCTCCTCTTTGACTCAGAGAAGAGAATGTGGACAACGGTTCATCC TGGAGCCAGAAAGATGAAAGAAAGTGGGAGAATGACAAGGTTGTGGCCATGTCCTTCCATT ACTTCTCAATGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGGCATGGACAGCACC CTGGAGCCAAGTGCAGGAGCACCACTCGCCATGTCCTCAGGCACAACCCAACTCAGGGCCAC AGCCACCACCCTCATCCTTTGCTGCCTCCTCATCATCCTCCCCTGCTTCATCCTCCCTGGCA TCTGAGGAGAGTCCTTTAGAGTGACAGGTTAAAGCTGATACCAAAAGGCTCCTGTGAGCACG GTCTTGATCAAACTCGCCCTTCTGTCTGGCCAGCTGCCCACGACCTACGGTGTATGTCCAGT GGCCTCCAGCAGATCATGATGACATCATGGACCCAATAGCTCATTCACTGCCTTGATTCCTT TTGCCAACAATTTTACCAGCAGTTATACCTAACATATTATGCAATTTTCTCTTGGTGCTACC GTCAGTAAAATAATCACGTTAGACTTCAGACCTCTGGGGATTCTTTCCGTGTCCTGAAAGAG AATTTTTAAATTATTAATAAGAAAAATTTATATTAATGATTGTTTCCTTTAGTAATTTAT

MAAAAATKILLCLPLLLLLSGWSRAGRADPHSLCYDITVIPKFRPGPRWCAVQGQVDEKTFL HYDCGNKTVTPVSPLGKKLNVTTAWKAQNPVLREVVDILTEQLRDIQLENYTPKEPLTLQAR MSCEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYFS MGDCIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLILCCLLIILPCFILPGI

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FIGURE 155

 ${\tt MELIPTITSWRVLILVVALTQFWCGFLCRGFHLQNHELWLLIKREFGFYSKSQYRTWQKKLA}$ ${\tt EDSTWPPINRTDYSGDGKNGFYINGGYESHEQIPKRKLKLGGQPTEQHFWARL}$

FIGURE 156

GTTCTCCTTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACCATGAAG CTCTTGTGGCAGGTAACTGTGCACCACCACCTGGAATGCCATCCTGCTCCCGTTCGTCTA CCTCACGGCGCAAGTGTGGATTCTGTGTGCAGCCATCGCTGCCGCCCTCAGCCGGGCCCC AGAACTGCCCCTCCGTTTGCTCGTGCAGTAACCAGTTCAGCAAGGTGGTGTGCACGCGCCGG GGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACCTCATGGAGAA CAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCACCTGGAGGTCCTGCAGT TGGGCAGGAACTCCATCCGGCAGATTGAGGTGGGGGCCTTCAACGGCCTGGCCAGCCTCAAC ACCCTGGAGCTGTTCGACAACTGGCTGACAGTCATCCCTAGCGGGGCCTTTGAATACCTGTC CAAGCTGCGGGAGCTCTGGCTTCGCAACAACCCCATCGAAAGCATCCCCTCTTACGCCTTCA ACCGGGTGCCCTCCTCATGCGCCTGGACTTGGGGGAGCTCAAGAAGCTGGAGTATATCTCT GAGGGAGCTTTTGAGGGGCTGTTCAACCTCAAGTATCTGAACTTGGGCATGTGCAACATTAA AGACATGCCCAATCTCACCCCCCTGGTGGGGGCTGGAGGAGCTGGAGATGTCAGGGAACCACT TCCCTGAGATCAGGCCTGGCTCCTTCCATGGCCTGAGCTCCCTCAAGAAGCTCTGGGTCATG CAACTTGGCCCACAATAACCTCTCTTCTTTGCCCCATGACCTCTTTACCCCGCTGAGGTACC TGGTGGAGTTGCATCTACACCACAACCCTTGGAACTGTGATTGTGACATTCTGTGGCTAGCC TGGTGGCTTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCCGCTGTCATGCTCCCAT GCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCCTTCCAGTGCTCTGCCCCCT TCATCATGGACGCACCTCGAGACCTCAACATTTCTGAGGGTCGGATGGCAGAACTTAAGTGT CGGACTCCCCTATGTCCTCCGTGAAGTGGTTGCTGCCCAATGGGACAGTGCTCAGCCACGC CTCCCGCCACCCAAGGATCTCTGTCCTCAACGACGGCACCTTGAACTTTTCCCACGTGCTGC TTTCAGACACTGGGGTGTACACATGCATGGTGACCAATGTTGCAGGCAACTCCAACGCCTCG GCCTACCTCAATGTGAGCACGGCTGAGCTTAACACCTCCAACTACAGCTTCTTCACCACAGT AACAGTGGAGACCACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCCTA CCACGTCCACTGGTTACCAGCCGGCATATACCACCTCTACCACGGTGCTCATTCAGACTACC CGTGTGCCCAAGCAGGTGGCAGTACCCGCGACAGACACCACTGACAAGATGCAGACCAGCCT GGATGAAGTCATGAAGACCACCAAGATCATCATTGGCTGCTTTGTGGCAGTGACTCTGCTAG CTGCCGCCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTC ACAGCCGCCCGGACTGTTGAGATAATCCAGGTGGACGAAGACATCCCAGCAGCAACATCCGC AGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTC ATGACCATATTAACTACAACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGC CTGGGGAACTCTCTGCACCCCACAGTCACCACTATCTCTGAACCTTATATAATTCAGACCCA GCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTA CAAAAAGTCAAAACA

FIGURE 157

MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAAASAGPQNCPSVCSCSNQFSKVVCT
RRGLSEVPQGIPSNTRYLNLMENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFNGLAS
LNTLELFDNWLTVIPSGAFEYLSKLRELWLRNNPIESIPSYAFNRVPSLMRLDLGELKKLEY
ISEGAFEGLFNLKYLNLGMCNIKDMPNLTPLVGLEELEMSGNHFPEIRPGSFHGLSSLKKLW
VMNSQVSLIERNAFDGLASLVELNLAHNNLSSLPHDLFTPLRYLVELHLHHNPWNCDCDILW
LAWWLREYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAEL
KCRTPPMSSVKWLLPNGTVLSHASRHPRISVLNDGTLNFSHVLLSDTGVYTCMVTNVAGNSN
ASAYLNVSTAELNTSNYSFFTTVTVETTEISPEDTTRKYKPVPTTSTGYQPAYTTSTTVLIQ
TTRVPKQVAVPATDTTDKMQTSLDEVMKTTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRS
TVTAARTVEIIQVDEDIPAATSAAATAAPSGVSGEGAVVLPTIHDHINYNTYKPAHGAHWTE
NSLGNSLHPTVTTISEPYIIQTHTKDKVQETQI

FIGURE 158

CGCTCGGGCACCAGCCGCGGCAAGGATGGAGCTGGGTTGCTGGACGCAGTTGGGGCTCACTT TTCTTCAGCTCCTTCTCATCTCGTCCTTGCCAAGAGAGTACACAGTCATTAATGAAGCCTGC CCTGGAGCAGAGTGGAATATCATGTGTCGGGAGTGCTGTGAATATGATCAGATTGAGTGCGT CTGCCCGGAAAGAGGGAAGTCGTGGGTTATACCATCCCTTGCTGCAGGAATGAGGAGAATG AGTGTGACTCCTGCCTGATCCACCCAGGTTGTACCATCTTTGAAAACTGCAAGAGCTGCCGA AATGGCTCATGGGGGGGTACCTTGGATGACTTCTATGTGAAGGGGTTCTACTGTGCAGAGTG CCGAGCAGGCTGGTACGGAGGAGACTGCATGCGATGTGGCCAGGTTCTGCGAGCCCCAAAGG GTCAGATTTTGTTGGAAAGCTATCCCCTAAATGCTCACTGTGAATGGACCATTCATGGTAAA CCTGGGTTTGTCATCCAACTAAGATTTGTCATGTTGAGTCTGGAGTTTGACTACATGTGCCA GTATGACTATGTTGAGGTTCGTGATGGAGACAACCGCGATGGCCAGATCATCAAGCGTGTCT GTGGCAACGAGCGCCAGCTCCTATCCAGAGCATAGGATCCTCACTCCACGTCCTCTTCCAC TCCGATGGCTCCAAGAATTTTGACGGTTTCCATGCCATTTATGAGGAGATCACAGCATGCTC CTCATCCCCTTGTTTCCATGACGGCACGTGCGTCCTTGACAAGGCTGGATCTTACAAGTGTG GACCCTGGGGGCCCAGTCAATGGGTACCAGAAAATAACAGGGGGCCCTGGGCTTATCAACGG ACGCCATGCTAAAATTGGCACCGTGGTGTCTTTCTTTTGTAACAACTCCTATGTTCTTAGTG GCAATGAGAAAAGAACTTGCCAGCAGAATGGAGAGTGGTCAGGGAAACAGCCCATCTGCATA AAAGCCTGCCGAGAACCAAAGATTTCAGACCTGGTGAGAAGGAGAGTTCTTCCGATGCAGGT AGAGTGCCCCTACCAAGAAGCCAGCCCTTCCCTTTGGAGATCTGCCCATGGGATACCAACAT CTGCATACCCAGCTCCAGTATGAGTGCATCTCACCCTTCTACCGCCGCCTGGGCAGCAGCAG GAGGACATGTCTGAGGACTGGGAAGTGGAGTGGGCGGCCACCATCCTGCATCCCTATCTGCG ATCTACAGGAGGACCAGCGGGGTGCATGACGGCAGCCTACACAAGGGAGCGTGGTTCCTAGT CTGCAGCGGTGCCCTGGTGAATGAGCGCACTGTGGTGGTGGTGGCCCACTGTGTTACTGACC TGGGGAAGGTCACCATGATCAAGACAGCAGACCTGAAAGTTGTTTTGGGGAAATTCTACCGG GATGATGACCGGGATGAGAAGACCATCCAGAGCCTACAGATTTCTGCTATCATTCTGCATCC CAACTATGACCCCATCCTGCTTGATGCTGACATCGCCATCCTGAAGCTCCTAGACAAGGCCC CAGGAGTCCCACATCACTGTGGCTGGCTGGAATGTCCTGGCAGACGTGAGGAGCCCTGGCTT CAAGAACGACACTGCGCTCTGGGGTGGTCAGTGTGGTGGACTCGCTGTGTGAGGAGC AGCATGAGGACCATGGCATCCCAGTGAGTGTCACTGATAACATGTTCTGTGCCAGCTGGGAA CCCACTGCCCCTTCTGATATCTGCACTGCAGAGACAGGAGGCATCGCGGCTGTGTCCTTCCC GGGACGAGCATCTCCTGAGCCACGCTGGCATCTGATGGGACTGGTCAGCTGGAGCTATGATA AAACATGCAGCCACAGGCTCTCCACTGCCTTCACCAAGGTGCTGCCTTTTAAAGACTGGATT GAAAGAAATATGAAA**TGA**ACCATGCTCATGCACTCCTTGAGAAGTGTTTCTGTATATCCGTC TGTACGTGTGTCATTGCGTGAAGCAGTGTGGGCCTGAAGTGTGATTTGGCCTGTGAACTTGG CTGTGCCAGGGCTTCTGACTTCAGGGACAAAACTCAGTGAAGGGTGAGTAGACCTCCATTGC TGGTAGGCTGATGCCGCGTCCACTACTAGGACAGCCAATTGGAAGATGCCAGGGCTTGCAAG AAGTAAGTTTCTTCAAAGAAGACCATATACAAAACCTCTCCACTCCACTGACCTGGTGGTCT TCCCCAACTTTCAGTTATACGAATGCCATCAGCTTGACCAGGGAAGATCTGGGCTTCATGAG GCCCTTTTGAGGCTCTCAAGTTCTAGAGAGCTGCCTGTGGGACAGCCCAGGGCAGCAGAGC

FIGURE 159

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAEWNIMCRECCEYDQIECVCPGKREVV
GYTIPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGTLDDFYVKGFYCAECRAGWYGGD
CMRCGQVLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRD
GDNRDGQIIKRVCGNERPAPIQSIGSSLHVLFHSDGSKNFDGFHAIYEEITACSSSPCFHDG
TCVLDKAGSYKCACLAGYTGQRCENLLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTV
VSFFCNNSYVLSGNEKRTCQQNGEWSGKQPICIKACREPKISDLVRRRVLPMQVQSRETPLH
QLYSAAFSKQKLQSAPTKKPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRRTCLRTGK
WSGRAPSCIPICGKIENITAPKTQGLRWPWQAAIYRRTSGVHDGSLHKGAWFLVCSGALVNE
RTVVVAAHCVTDLGKVTMIKTADLKVVLGKFYRDDDRDEKTIQSLQISAIILHPNYDPILLD
ADIAILKLLDKARISTRVQPICLAASRDLSTSFQESHITVAGWNVLADVRSPGFKNDTLRSG
VVSVVDSLLCEEQHEDHGIPVSVTDNMFCASWEPTAPSDICTAETGGIAAVSFPGRASPEPR
WHLMGLVSWSYDKTCSHRLSTAFTKVLPFKDWIERNMK

FIGURE 160

ACCAGGCATTGTATCTTCAGTTGTCATCAAGTTCGCAATCAGATTGGAAAAGCTCAACTTGA AGCTTTCTTGCCTGCAGTGAAGCAGAGAGATAGATATTATTCACGTAATAAAAAACATGGGC TTCAACCTGACTTTCCACCTTTCCTACAAATTCCGATTACTGTTGCTGTTGACTTTGTGCCT GACAGTGGTTGGGTGGGCCACCAGTAACTACTTCGTGGGTGCCATTCAAGAGATTCCTAAAG CAAAGGAGTTCATGGCTAATTTCCATAAGACCCTCATTTTGGGGAAGGGAAAAACTCTGACT AATGAAGCATCCACGAAGAAGGTAGAACTTGACAACTGTCCTTCTGTGTCTCCTTACCTCAG AGGCCAGAGCAAGCTCATTTTCAAACCAGATCTCACTTTGGAAGAGGTACAGGCAGAAAATC CCAAAGTGTCCAGAGGCCGGTATCGCCCTCAGGAATGTAAAGCTTTACAGAGGGTCGCCATCCTC GTTCCCCACCGGAACAGAGAGAAACACCTGATGTACCTGCTGGAACATCTGCATCCCTTCCT GCAGAGGCAGCTGGATTATGGCATCTACGTCATCCACCAGGCTGAAGGTAAAAAGTTTA ATCGAGCCAAACTCTTGAATGTGGGCTATCTAGAAGCCCTCAAGGAAGAAAATTGGGACTGC TTTATATTCCACGATGTGGACCTGGTACCCGAGAATGACTTTAACCTTTACAAGTGTGAGGA GCATCCCAAGCATCTGGTGGTTGGCAGGAACAGCACTGGGTACAGGTTACGTTACAGTGGAT ATTTTGGGGGTGTTACTGCCCTAAGCAGAGAGCAGTTTTTCAAGGTGAATGGATTCTCTAAC AACTACTGGGGATGGGGAGGCGAAGACGATGACCTCAGACTCAGGGTTGAGCTCCAAAGAAT GAAAATTTCCCGGCCCCTGCCTGAAGTGGGTAAATATACAATGGTCTTCCACACTAGAGACA AAGGCAATGAGGTGAACGCAGAACGGATGAAGCTCTTACACCAAGTGTCACGAGTCTGGAGA ACAGATGGGTTGAGTAGTTCTTATAAATTAGTATCTGTGGAACACAATCCTTTATATAT CAACATCACAGTGGATTTCTGGTTTGGTGCATGACCCTGGATCTTTTGGTGATGTTTGGAAG AACTGATTCTTTGCTTTGCAATAATTTTGGCCTAGAGACTTCAAATAGTAGCACACATTAAGA ACCTGTTACAGCTCATTGTTGAGCTGAATTTTTCCTTTTTGTATTTTCTTAGCAGAGCTCCT GGTGATGTAGAGTATAAAACAGTTGTAACAAGACAGCTTTCTTAGTCATTTTGATCATGAGG GTTAAATATTGTAATATGGATACTTGAAGGACTTTATATAAAAGGATGACTCAAAGGATAAA GGGATAAAAGGCCACAGGAAATAAGACTGCTGAATGTCTGAGAGAACCAGAGTTGTTCTCGT CCAAGGTAGAAAGGTACGAAGATACAATACTGTTATTCATTTATCCTGTACAATCATCTGTG AAGTGGTGGTGTCAGGTGAGAAGGCGTCCACAAAAGAGGGGAGAAAAGGCGACGAATCAGGA CACAGTGAACTTGGGAATGAAGAGGTAGCAGGAGGTGGAGTGTCGGCTGCAAAGGCAGCAG TAGCTGAGCTGCTTGCAGGTGCTGATAGCCTTCAGGGGAGGACCTGCCCAGGTATGCCTTCC AGTGATGCCCACCAGAGAATACATTCTCTATTAGTTTTTAAAGAGTTTTTGTAAAATGATTT TGTACAAGTAGGATATGAATTAGCAGTTTACAAGTTTACATATTAACTAATAATAATATGT CTATCAAATACCTCTGTAGTAAAATGTGAAAAAGCAAAA

ر (4/310 FIGURE 161

MGFNLTFHLSYKFRLLLLLTLCLTVVGWATSNYFVGAIQEIPKAKEFMANFHKTLILGKGKT LTNEASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRV AILVPHRNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEGKKFNRAKLLNVGYLEALKEEN WDCFIFHDVDLVPENDFNLYKCEEHPKHLVVGRNSTGYRLRYSGYFGGVTALSREQFFKVNG FSNNYWGWGGEDDDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSR VWRTDGLSSCSYKLVSVEHNPLYINITVDFWFGA

Important features:

Signal peptide:

amino acids 1-27

N-glycosylation sites:

amino acids 4-7, 220-223 and 335-338

Xylose isomerase proteins:

amino acids 191-201

FIGURE 162

CGTGGGCCGGGGTCGCGCAGCGGGCTGTGGGCGCCCCGGAGGAGCGACCGCCGCAGTTCTC GAGCTCCAGCTGCATTCCCTCCGCGTCCGCCCCACGCTTCTCCCGCTCCGGGCCCCGCAATG CCCGCCAGGGTGGCCGCAGGCCTGTATGAACTCAATCTCACCACCGATAGCCCTGCCACCA CGGGAGCGGTGGTGACCATCTCGGCCAGCCTGGTGGCCAAGGACAACGGCAGCCTGGCCCTG CCCGCTGACGCCCACCTCTACCGCTTCCACTGGATCCACACCCCGCTGGTGCTTACTGGCAA GATGGAGAAGGGTCTCAGCTCCACCATCCGTGTGGTCGGCCACGTGCCCGGGGAATTCCCGG TCTCTGTCTGGGTCACTGCCGCTGACTGCTGGATGTGCCAGCCTGTGGCCAGGGGCTTTGTG GTCCTCCCATCACAGAGTTCCTCGTGGGGGACCTTGTTGTCACCCAGAACACTTCCCTACC GCAACTTCCTCAAGACCGCCTTGTTTCTCTACAGCTGGGACTTCGGGGACGGGACCCAGATG GTGACTGAAGACTCCGTGGTCTATTATAACTATTCCATCATCGGGACCTTCACCGTGAAGCT CAAAGTGGTGGCGGAGTGGGAAGAGGTGGAGCCGGATGCCACGAGGGCTGTGAAGCAGAAGA CCGGGGACTTCTCCGCCTCGCTGAAGCTGCAGGAAACCCTTCGAGGCATCCAAGTGTTGGGG CCCACCTAATTCAGACCTTCCAAAAGATGACCGTGACCTTGAACTTCCTGGGGAGCCCTCC TCTGACTGTGTGCTGGCGTCTCAAGCCTGAGTGCCTCCCGCTGGAGGAAGGGGAGTGCCACC CTGTGTCCGTGGCCAGCACAGCGTACAACCTGACCCACACCTTCAGGGACCCTGGGGACTAC TGCTTCAGCATCCGGGCCGAGAATATCATCAGCAAGACACATCAGTACCACAAGATCCAGGT GTGGCCCTCCAGAATCCAGCCGGCTGTCTTTGCTTTCCCATGTGCTACACTTATCACTGTGA TGTTGGCCTTCATCATGTACATGACCCTGCGGAATGCCACTCAGCAAAAGGACATGGTGGAG AACCCGGAGCCACCCTCTGGGGTCAGGTGCTGCCAGATGTGCTGTGGGCCTTTCTTGCT GGAGACTCCATCTGAGTACCTGGAAATTGTTCGTGAGAACCACGGGCTGCTCCCGCCCCTCT ATAAGTCTGTCAAAACTTACACCGTGTGAGCACTCCCCCTCCCCACCCCATCTCAGTGTTAA CTGACTGCTGACTTGGAGTTTCCAGCAGGGTGGTGTGCACCACTGACCAGGAGGGGTTCATT TGCGTGGGGCTGTTGGCCTGGATCATCCATCCATCTGTACAGTTCAGCCACTGCCACAAGCC CCTCCCTCTCTGTCACCCCTGACCCCAGCCATTCACCCATCTGTACAGTCCAGCCACTGACA TAAGCCCCACTCGGTTACCACCCCCTTGACCCCTACCTTTGAAGAGGCTTCGTGCAGGACT TTGATGCTTGGGGTGTTCCGTGTTGACTCCTAGGTGGGCCTGGCTGCCCACTGCCCATTCCT CTCATATTGGCACATCTGCTGTCCATTGGGGGTTCTCAGTTTCCTCCCCCAGACAGCCCTAC CTGTGCCAGAGAGCTAGAAAGAAGGTCATAAAGGGTTAAAAAATCCATAACTAAAGGTTGTAC CACACACACAGAAATATAAACACATGCGTCACATGGGCATTTCAGATGATCAGCTCTGTA TCTGGTTAAGTCGGTTGCTGGGATGCACCCTGCACTAGAGCTGAAAGGAAATTTGACCTCCA AGCAGCCCTGACAGGTTCTGGGCCCGGGCCCTCCCTTTGTGCTTTGTCTCTGCAGTTCTTGC GCCCTTTATAAGGCCATCCTAGTCCCTGCTGGCTGGCAGGGGCCTGGATGGGGGGCAGGACT AATACTGAGTGATTGCAGAGTGCTTTATAAATATCACCTTATTTTATCGAAACCCATCTGTG AAACTTTCACTGAGGAAAAGGCCTTGCAGCGGTAGAAGAGGTTGAGTCAAGGCCGGGCGCG TGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCACGAGATCAGGA AGCCGGGCGTGGTGGTGGCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG GTGCGAACCCGGGAGGCGGAGCTTGCAGTGAGCCCAGATGGCGCCACTGCACTCCAGCCTGA **GTGACAGAGCGAGACTCTGTCTCCA**

76/310 FIGURE 163

MAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPATTGAVVTISASLVAKDNGSLA
LPADAHLYRFHWIHTPLVLTGKMEKGLSSTIRVVGHVPGEFPVSVWVTAADCWMCQPVARGF
VVLPITEFLVGDLVVTQNTSLPWPSSYLTKTVLKVSFLLHDPSNFLKTALFLYSWDFGDGTQ
MVTEDSVVYYNYSIIGTFTVKLKVVAEWEEVEPDATRAVKQKTGDFSASLKLQETLRGIQVL
GPTLIQTFQKMTVTLNFLGSPPLTVCWRLKPECLPLEEGECHPVSVASTAYNLTHTFRDPGD
YCFSIRAENIISKTHQYHKIQVWPSRIQPAVFAFPCATLITVMLAFIMYMTLRNATQQKDMV
ENPEPPSGVRCCCQMCCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV

Important features of the protein:

Signal peptide:

amino acids 1-24

Transmembrane domain:

amino acids 339-362

N-glycosylation sites.

amino acids 34-37, 58-61, 142-145, 197-200, 300-303 and 364-367

FIGURE 164

168/>10 FIGURE 165

MALSSQIWAACLLLLLLASLTSGSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRRDTH FPICIFCCGCCHRSKCGMCCKT

FIGURE 166

CTGTCAGGAAGGACCATCTGAAGGCTGCAATTTGTTCTTAGGGAGGCAGGTGCTGGCCTGGC CTGGATCTTCCACCATGTTCCTGTTGCTGCCTTTTGATAGCCTGATTGTCAACCTTCTGGGC AGTCTCCTTTGGTATCCGCAAACTCTACATGAAAAGTCTGTTAAAAATCTTTGCGTGGGCTA CCTTGAGAATGGAGCGAGGAGCCAAGGAGAAGAACCACCAGCTTTACAAGCCCTACACCAAC GGAATCATTGCAAAGGATCCCACTTCACTAGAAGAAGAGATCAAAGAGATTCGTCGAAGTGG TAGTAGTAAGGCTCTGGACAACACTCCAGAGTTCGAGCTCTCTGACATTTTCTACTTTTGCC GGAAAGGAATGGAGACCATTATGGATGATGAGGTGACAAAGAGATTCTCAGCAGAAGAACTG GAGTCCTGGAACCTGCTGAGCAGAACCAATTATAACTTCCAGTACATCAGCCTTCGGCTCAC GGTCCTGTGGGGGTTAGGAGTGCTGATTCGGTACTGCTTTCTGCTGCCGCTCAGGATAGCAC TGGCTTTCACAGGGATTAGCCTTCTGGTGGTGGGCACAACTGTGGTGGGATACTTGCCAAAT AGCGCTGACAGCCATCATCACCATGACAGGGAAAACAGACCAAGAAATGGTGGCATCT GTGTGGCCAATCATACCTCACCGATCGATGTGATCATCTTGGCCAGCGATGGCTATTATGCC ATGGTGGGTCAAGTGCACGGGGGACTCATGGGTGTGATTCAGAGAGCCATGGTGAAGGCCTG CCCACACGTCTGGTTTGAGCGCTCGGAAGTGAAGGATCGCCACCTGGTGGCTAAGAGACTGA CTGAACATGTGCAAGATAAAAGCAAGCTGCCTATCCTCATCTTCCCAGAAGGAACCTGCATC AATAATACATCGGTGATGATGTTCAAAAAGGGAAGTTTTGAAATTGGAGCCACAGTTTACCC TGTTGCTATCAAGTATGACCCTCAATTTGGCGATGCCTTCTGGAACAGCAGCAAATACGGGA TGGTGACGTACCTGCGAATGATGACCAGCTGGGCCATTGTCTGCAGCGTGTGGTACCTG CCTCCCATGACTAGAGAGGCAGATGAAGATGCTGTCCAGTTTGCGAATAGGGTGAAATCTGC CATTGCCAGGCAGGAGGACTTGTGGACCTGCTGTGGGATGGGGGCCTGAAGAGGGAGAAGG TGAAGGACACGTTCAAGGAGGAGCAGCAGAAGCTGTACAGCAAGATGATCGTGGGGAACCAC AAGGACAGGAGCCGCTCCTGAGCCTCCAGCTGGCTGGGGCCACCGTGCGGGGTGCCAA CGGGCTCAGAGCTGGAGTTGCCGCCGCCCCCCCCCCTGTGTCCTTTCCAGACTCCAGGG CTCCCGGGCTGCTCTGGATCCCAGGACTCCGGCTTTCGCCGAGCCGCAGCGGGATCCCTGT GCACCCGGCGCAGCCTACCCTTGGTGGTCTAAACGGATGCTGCTGGGTGTTGCGACCCAGGA CGAGATGCCTTGTTTCTTTTACAATAAGTCGTTGGAGGAATGCCATTAAAGTGAACTCCCCA CCTTTGCACGCTGTGCGGGTGAGTGGTTGGGGAGATGTGGCCATGGTCTTGTGCTAGAGAT GGCGGTACAAGAGTCTGTTATGCAAGCCCGTGTGCCAGGGATGTGCTGGGGGGGCGCCACCCG CTCTCCAGGAAAGGCACAGCTGAGGCACTGTGGCTGGCTTCGGCCTCAACATCGCCCCCAGC CTTGGAGCTCTGCAGACATGATAGGAAGGAAACTGTCATCTGCAGGGGCTTTCAGCAAAATG GGCCGCTGACTGGGCCATGGGGAGAACGTGTTCGTACTCCAGGCTAACCCTGAACTCCCC ATGTGATGCGCGCTTTGTTGAATGTGTGTCTCGGTTTCCCCATCTGTAATATGAGTCGGGGG AGGACACATCACGTTCAGTGTTTCAAGTACAGGCCCACAAAACGGGGCACGGCAGGCCTGAG

140/310 FIGURE 167

MFLLLPFDSLIVNLLGISLTVLFTLLLVFIIVPAIFGVSFGIRKLYMKSLLKIFAWATLRME
RGAKEKNHQLYKPYTNGIIAKDPTSLEEEIKEIRRSGSSKALDNTPEFELSDIFYFCRKGME
TIMDDEVTKRFSAEELESWNLLSRTNYNFQYISLRLTVLWGLGVLIRYCFLLPLRIALAFTG
ISLLVVGTTVVGYLPNGRFKEFMSKHVHLMCYRICVRALTAIITYHDRENRPRNGGICVANH
TSPIDVIILASDGYYAMVGQVHGGLMGVIQRAMVKACPHVWFERSEVKDRHLVAKRLTEHVQ
DKSKLPILIFPEGTCINNTSVMMFKKGSFEIGATVYPVAIKYDPQFGDAFWNSSKYGMVTYL
LRMMTSWAIVCSVWYLPPMTREADEDAVQFANRVKSAIARQGGLVDLLWDGGLKREKVKDTF
KEEQQKLYSKMIVGNHKDRSRS

_\\$^1/3\0 FIGURE 168

GCCCTCGAAACCAGGACTCCAGCACCTCTGGTCCCGCCCTCACCCGGACCCCTGGCCCTCA CGTCTCCTCCAGGGATGGCGCTGGCGGCTTTGATGATCGCCCTCGGCAGCCTCGGCCTCCAC ACCTGGCAGGCCAGGCTGTTCCCACCATCCTGCCCCTGGGCCTGGCTCCAGACACCTTTGA CGATACCTATGTGGGTTGTGCAGAGGAGATGGAGGAGAAGGCAGCCCCCTGCTAAAGGAGG **AAATGGCCCACCATGCCCTGCTGCGGAATCCTGGGAGGCAGCCCAGGAGACCTGGGAGGAC** AAGCGTCGAGGGCTTACCTTGCCCCCTGGCTTCAAAGCCCAGAATGGAATAGCCATTATGGT CTACACCAACTCATCGAACACCTTGTACTGGGAGTTGAATCAGGCCGTGCGGACGGGCGGAG GCTCCCGGGAGCTCTACATGAGGCACTTTCCCTTCAAGGCCCTGCATTTCTACCTGATCCGG GCCCTGCAGCTGCGAGGCAGTGGGGGGCTGCAGCAGGGGACCTGGGGAGGTGGTGTTCCG AGGTGTGGGCAGCCTTCGCTTTGAACCCAAGAGGCTGGGGGACTCTGTCCGCTTGGGCCAGT TTGCCTCCAGCTCCCTGGATAAGGCAGTGGCCCACAGATTTGGGGAGAAGAGGCGGGGCTGT GTGTCTGCGCCAGGGGTGCAGCTAGGGTCACAATCTGAGGGGGCCTCCTCTCTGCCCCCCTG GAAGACTCTGCTCTTGGCCCCTGGAGAGTTCCAGCTCTCAGGGGTTGGGCCCTGAAAGTCCA ACATCTGCCACTTAGGAGCCCTGGGAACGGGTGACCTTCATATGACGAAGAGGCACCTCCAG CAGCCTTGAGAAGCAAGAACATGGTTCCGGACCCAGCCCTAGCAGCCTTCTCCCCAACCAGG ATGTTGGCCTGGGGAGGCCACAGCAGGGCTGAGGGAACTCTGCTATGTGATGGGGACTTCCT TGGAGTTTTATTGAGGTAGCTACGTGATTAAATGGTATTGCAGTGTGGA

ノキとかい FIGURE 169

MALAALMIALGSLGLHTWQAQAVPTILPLGLAPDTFDDTYVGCAEEMEEKAAPLLKEEMAHH
ALLRESWEAAQETWEDKRRGLTLPPGFKAQNGIAIMVYTNSSNTLYWELNQAVRTGGGSREL
YMRHFPFKALHFYLIRALQLLRGSGGCSRGPGEVVFRGVGSLRFEPKRLGDSVRLGQFASSS
LDKAVAHRFGEKRRGCVSAPGVQLGSQSEGASSLPPWKTLLLAPGEFQLSGVGP

イギジ/ついつ FIGURE 170

GTGGCTTCATTTCAGTGGCTGACTTCCAGAGAGCAATATGGCTGGTTCCCCAACATGCCTCA CCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTG GTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTCCAAAGTAAAGCAAGTTGACTC TATTGTCTGGACCTTCAACACCCCCTCTTGTCACCATACAGCCAGAAGGGGGCCACTATCA TAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAG CTCAGCAAACTGAAGAAGAATGACTCAGGGATCTACTATGTGGGGATATACAGCTCATCACT CCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAG TCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATG GAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCTGGGGCAAGCAGCCAATGAGTC CCATAATGGGTCCATCCTCCCATCTCCTGGAGATGGGGAGAAAGTGATATGACCTTCATCT GCGTTGCCAGGAACCCTGTCAGCAGAAACTTCTCAAGCCCCATCCTTGCCAGGAAGCTCTGT GAAGGTGCTGATGACCCAGATTCCTCCATGGTCCTCCTGTGTCTCCTGTTGGTGCCCCT AGTACATTGAAGAGAAGAGAGAGTGGACATTTGTCGGGAAACTCCTAACATATGCCCCCAT TCTGGAGAGACACAGAGTACGACACAATCCCTCACACTAATAGAACAATCCTAAAGGAAGA TCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAAAGATGGAAAATCCCCACTCAC TGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAGAATGTTATC<u>TAG</u>ACAGCAGTG CACTCCCCTAAGTCTCTGCTCA

174/510 FIGURE 171

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVT
IQPEGGTIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHV
YEHLSKPKVTMGLQSNKNGTCVTNLTCCMEHGEEDVIYTWKALGQAANESHNGSILPISWRW
GESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLW
FLKRERQEEYIEEKKRVDICRETPNICPHSGENTEYDTIPHTNRTILKEDPANTVYSTVEIP
KKMENPHSLLTMPDTPRLFAYENVI

ペキ5/つへつ FIGURE 172

CTGGTTCCCCAACATGCCTCACCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCC TCTGGACCCGTGAAAGAGCTGGTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTC CAAAGTAAAGCAAGTTGACTCTATTGTCTGGACCTTCAACACAACCCCTCTTGTCACCATAC AGCCAGAAGGGGGCACTATCATAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCA GATGGAGGCTACTCCCTGAAGCTCAGCAAACTGAAGAAGAATGACTCAGGGATCTACTATGT GGGGATATACAGCTCATCACTCCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACG AGCACCTGTCAAAGCCTAAAGTCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTG ACCAATCTGACATGCTGCATGGAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCT GGGGCAAGCAGCCAATGAGTCCCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAG AAAGTGATATGACCTTCATCTGCGTTGCCAGGAACCCTGTCAGCAGAAACTTCTCAAGCCCC ATCCTTGCCAGGAAGCTCTGTGAAGGTGCTGCTGATGACCCAGATTCCTCCATGGTCCTCCT GTGTCTCCTGTTGGTGCCCCTCCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTC ACTCCTAACATATGCCCCCATTCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAA TAGAACAATCCTAAAGGAAGATCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAA AGATGGAAAATCCCCACTCACTGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAG

-176/310 FIGURE 173

MKMLLLLCLGLTLVCVHAEEASSTGRNFNVEKINGEWHTIILASDKREKIEEHGNFRLFLEQ IHVLENSLVLKVHTVRDEECSELSMVADKTEKAGEYSVTYDGFNTFTIPKTDYDNFLMAHLI NEKDGETFQLMGLYGREPDLSSDIKERFAQLCEEHGILRENIIDLSNANRCLQARE

FIGURE 175

トラ/シハロ FIGURE 176

MTCCEGWTSCNGFSLLVLLLLGVVLNAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMA
IPATTMSLTARKRACCNNRTGMFLSSFFSVITVIGALYCMLISIQALLKGPLMCNSPSNSNA
NCEFSLKNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSFHFDSEENKHRL
IHFSVFLGLLLVGILEVLFGLSQIVIGFLGCLCGVSKRRSQIV

180/510 FIGURE 177

GTCGAATCCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACCATGATGAGGCT
GTCAGTGTGTCTCCTGATGGTCTCGCTGGCCCTTTGCTGCTACCAGGCCCATGCTCTTGTCT
GCCCAGCTGTTGCTTCTGAGATCACAGTCTTCTTATTCTTAAGTGACGCTGCGGTAAACCTC
CAAGTTGCCAAACTTAATCCACCTCCAGAAGCTCTTGCAGCCAAGTTGGAAGTGAAGCACTG
CACCGATCAGATATCTTTTAAGAAACGACTCTCATTGAAAAAGTCCTGGTGGAAATAGTGAA
AAAATGTGGTGTGTGACATGTAAAAATGCTCAACCTGGTTTCCAAAGTCTTTCAACGACACC
CTGATCTTCACTAAAAATTGTAAAGGTTTCAACACGTTGCTTTAATAAATCACTTGCCCTGC

18:1/310 FIGURE 178

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEV KHCTDQISFKKRLSLKKSWWK

અ 8.2/১/১০ FIGURE 179

183/310 FIGURE 180

 ${\tt MERVTLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAGIAAVLSGKCK} \\ {\tt YKSSQKQHSPVPEKAIPLITPGSATTC}$

WO 99/63088 PCT/US99/12252

FIGURE 181

GGAGAAGAGGTTGTGTGGGACAAGCTGCTCCCGACAGAAGG<u>ATG</u>TCGCTGCTGAGCCTGCCC TGGCTGGGCCTCAGACCGGTGGCAATGTCCCCATGGCTACTCCTGCTGCTGGTTGTGGGCTC CTGGCTACTCGCCCGCATCCTGGCTTGGACCTATGCCTTCTATAACAACTGCCGCCGGCTCC AGTGTTTCCCACAGCCCCCAAAACGGAACTGGTTTTGGGGTCACCTGGGCCTGATCACTCCT ACAGAGGAGGCTTGAAGGACTCGACCCAGATGTCGGCCACCTATTCCCAGGGCTTTACGGT ATGGCTGGGTCCCATCATCCCCTTCATCGTTTTATGCCACCCTGACACCATCCGGTCTATCA CCAATGCCTCAGCTGCCATTGCACCCAAGGATAATCTCTTCATCAGGTTCCTGAAGCCCTGG CTGGGAGAGGGATACTGCTGAGTGGCGGTGACAAGTGGAGCCGCCACCGTCGGATGCTGAC GCCCGCCTTCCATTTCAACATCCTGAAGTCCTATATAACGATCTTCAACAAGAGTGCAAACA TCATGCTTGACAAGTGGCAGCACCTGGCCTCAGAGGGCAGCAGTCGTCTGGACATGTTTGAG CACATCAGCCTCATGACCTTGGACAGTCTACAGAAATGCATCTTCAGCTTTGACAGCCATTG TCAGGAGAGGCCCAGTGAATATATTGCCACCATCTTGGAGCTCAGTGCCCTTGTAGAGAAAA GAAGCCAGCATATCCTCCAGCACATGGACTTTCTGTATTACCTCTCCCATGACGGCGGCGC TTCCACAGGGCCTGCCGCCTGGTGCATGACTTCACAGACGCTGTCATCCGGGAGCGGCGTCG CACCCTCCCCACTCAGGGTATTGATGATTTTTTCAAAGACAAAGCCAAGTCCAAGACTTTGG ATTTCATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGGCATTGTCAGATGAGGAT ATAAGAGCAGAGGCTGACACCTTCATGTTTGGAGGCCATGACACCACGGCCAGTGGCCTCTC $\tt CTGGGTCCTGTACAACCTTGCGAGGCACCCAGAATACCAGGAGCGCTGCCGACAGGAGGTGC$ AAGAGCTTCTGAAGGACCGCGATCCTAAAGAGATTGAATGGGACGACCTGGCCCAGCTGCCC TTCCTGACCATGTGCGTGAAGGAGCCTGAGGTTACATCCCCCAGCTCCCTTCATCTCCCG ATGCTGCACCCAGGACATTGTTCTCCCAGATGGCCGAGTCATCCCCAAAGGCATTACCTGCC TCATCGATATTATAGGGGTCCATCACAACCCAACTGTGTGGCCGGATCCTGAGGTCTACGAC CCCTTCCGCTTTGACCCAGAGAACAGCAAGGGGGGGGTCACCTCTGGCTTTTATTCCTTTCTC CGCAGGGCCCAGGAACTGCATCGGGCAGGCGTTCGCCATGGCGGAGATGAAAGTGGTCCTGG CGTTGATGCTGCACTTCCGGTTCCTGCCAGACCACTGAGCCCCGCAGGAAGCTGGAA TTGATCATGCGCGCCGAGGGCGGCTTTGGCTGCGGGTGGAGCCCCTGAATGTAGGCTTGCA G<u>TGA</u>CTTTCTGACCCATCCACCTGTTTTTTTGCAGATTGTCATGAATAAAACGGTGCTGTCAAA

→85/310 FIGURE 182

MSLLSLPWLGLRPVAMSPWLLLLLVVGSWLLARILAWTYAFYNNCRRLQCFPQPPKRNWFWG
HLGLITPTEEGLKDSTQMSATYSQGFTVWLGPIIPFIVLCHPDTIRSITNASAAIAPKDNLF
IRFLKPWLGEGILLSGGDKWSRHRRMLTPAFHFNILKSYITIFNKSANIMLDKWQHLASEGS
SRLDMFEHISLMTLDSLQKCIFSFDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYY
LSHDGRRFHRACRLVHDFTDAVIRERRRTLPTQGIDDFFKDKAKSKTLDFIDVLLLSKDEDG
KALSDEDIRAEADTFMFGGHDTTASGLSWVLYNLARHPEYQERCRQEVQELLKDRDPKEIEW
DDLAQLPFLTMCVKESLRLHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVW
PDPEVYDPFRFDPENSKGRSPLAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHT
EPRRKLELIMRAEGGLWLRVEPLNVGLQ

へき6/310 FIGURE 183

→87/>\0 FIGURE 184

 ${\tt MYKLASCCLLFTGFLNPLLSLPLLDSREISFQLSAPHEDARLTPEELERASLLQILPEMLGA} \\ ERGDILRKADSSTNIFNPRGNLRKFQDFSGQDPNILLSHLLARIWKPYKKRETPDCFWKYCV$

FIGURE 185

189/310 FIGURE 186

 ${\tt MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDG}$ ${\tt GQAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO}$

CGGCCACAGCTGGCATGCTCTGCCTGATCGCCATCCTGCTGTATGTCCTCGTCCAGTACCTC GTGAACCCCGGGGTGCTCCGCACGGACCCCAGATGTCAAGAATATGAACACGTGGCTGCTGT TCCTCCCCTGTTCCCGGTGCAGGTGCAGACCCTGATAGTCGTGATCATCGGGATGCTCGTG CTCCTGCTGGACTTTCTTGGCTTGGTGCACCTGGGCCAGCTGCTCATCTTCCACATCTACCT GAGTATGTCCCCCACCTAAGCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATC TTACACCTCTACTTGAGTATGTCCCTAACCCTGAGCCCCCACGCCTGGGGCCAGAGTCTTT GTCCCCGTGTGCGCATGTGTTCAGGGTCAGCCTCTCCCAGAAGTGAGATCATGGACAAAAA GGGCAAATCACAGGAAGAAATTAAATCCATGAGGACCCAGCAGGCCCAGCAAGAAGCTGAAC TCACGCCGAGACCTGCAGGAGTGGTGCCAGGTGCT<u>TGA</u>AGTAACAAGTTTAAAATGTTCAGA GACAATGGAATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTT AACAACTGAAGCGAGAGCTGTGGTCTTGCTTGGTCTCACAGTGGGCACAGCGGTAGGCGGTC AGTCATGTTGCTGAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACCTGTGTTGGAAGT AACAACAACCTCCCTGCTCCTGGCACCAGCCGTTTTGGTCATGGTGGGCCAGCTGCAAAGCG ${\tt TCTTCCATTCTCTGGGCAGTGGTGGCCCCGAGGCTGTGGCCTCTCAGGGGGTTTCTGTGGAC}$ ACGGGCAGCAGAGTGTGTCCAGGCCAGCCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCA ACCCCTGGTCAGGGCAGAGGGAGTTGGGTGGGTCAGGCTCTGGGCTCACCTCCATCTCCAGA GCATCCCTGCCTGCAGTTGTGGCAAGAACGCCCAGCTCAGAATGAACACCCCCACCAAGA GCCTCCTTGTTCATAACCACAGGTTACCCTACAAACCACTGTCCCCACACAACCCTGGGGAT GTTTTAAAACACACCTCTAACGCATATCTTACAGTCACTGTTGTCTTGCCTGAGGGTTGA ATTTTTTTTAATGAAAGTGCAATGAAAATCACTGGATTAAATCCTACGGACACAGAGCTGAA

194/310 FIGURE 188

MNTWLLFLPLFPVQVQTLIVVIIGMLVLLLDFLGLVHLGQLLIFHIYLSMSPTLSPRSPQGW VVRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQ AQQEAELTPRPAGVVPGA

FIGURE 189

GGAGTGCAGATGGCATCCTTCGGTTCTTCCAGACAAGCTGCAAGACGCTGACCATGGCCAAG ATGGAGCTCTCGAAGGCCTTCTCTGGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCT ATCACTCAGCTTCTCCACAACATCCCTGCTCAGCAACTACTGGTTTGTGGGCCACACAGAAGG TGCCCAAGCCCTGTGCGAGAAAGGTCTGGCAGCCAAGTGCTTTGACATGCCAGTGTCCCTG GATGGAGATACCAACACATCCACCCAGGAGGTGGTACAATACAACTGGGAGACTGGGGATGA CCGGTTCTCCTTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAAACTGTGGAAG AACCAGGGGAGAGTGCCGAAGTTTCATTGAACTTACACCACCAGCCAAGAGAGGTGAGAAA GGACTACTGGAATTTGCCACGTTGCAAGGCCCATGTCACCCCACTCTCCGATTTGGAGGGAA GCGGTTGATGGAGAAGGCTTCCCTCCCCTCCCCTTGGGGCTTTGTGGCAAAAATCCTA TGGTTATCCCTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCTCCTGCT ACTAACAGACTTGCTACTCACTGGGAACCCTGCCTGTGGGCTCAAACTGAGCGCCTTTGCTG CTGTTTCCTCTGTCAGGTCTCCTGGGGATGGTGGCCCACATGATGTATTCACAAGTC TTCCAAGCGACTGTCAACTTGGGTCCAGAAGACTGGAGACCACATGTTTGGAATTATGGCTG ${\tt GGCCTTCTACATGGCCTGGCTCTCCTTCACCTGCTGCATGGCGTCGGCTGTCACCACCTTCA}$ ${\tt ACACGTACACCAGGATGGTGCTGGAGTTCAAGTGCAAGCA}{\tt TAG}{\tt TAAGAGCTTCAAGGAAAAC}$ ${\tt CCGAACTGCCTACCACCATCACCATCAGTGTTTCCCTCGGCGGCTGTCAAGTGCAGCCCCCAC}$ CGTGGGTCCTTTGACCAGCTACCACCAGTATCATAATCAGCCCATCCACTCTGTCTCTGAGG AAAGAAGCAGTTAGGTCATCTGTAGAGGAAGAGCAGTGTTAGGAGTTAAGCGGGTTTGGGGA GTAGGCTTGAGCCCTACCTTACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCG TCTCTTGAGCATGGTTTTTAGAGGCTACGAATAAGGCTATGAATAAGGGTTATCTTTAAGTC CTAAGGGATTCCTGGGTGCCACTGCTCTTTTCCTCTACAGCTCCATCTTGTTTCACCCAC CCCACATCTCACACATCCAGAATTCCCTTCTTTACTGATAGTTTCTGTGCCAGGTTCTGGGC TAAACCATGGAGATAAAAAGAAGAGTAAAATACACTTCCCGACCTTAAGGATCTGAAA

رير FIGURE 190

MAKMELSKAFSGQRTLLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGLAAKCFDMP
VSLDGDTNTSTQEVVQYNWETGDDRFSFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKR
GEKGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPPLGLCGKNPMVIPGNADHLHRTSIHQL
PPATNRLATHWEPCLWAQTERLCCCFLCPVRSPGDGGPHDVFTSLPSDCQLGSRRLETTCLE
LWLGLLHGLALLHLLHGVGCHHLQHVHQDGAGVQVQA

194/310 FIGURE 191

AACTGGAAGGAAAGAAAGGTCAGCTTTGGCCCAG<u>ATG</u>TGGTTACCCCTTGGTCTCCTG TCTTTATGTCTTTCTCCTCTTCCTATTCTGTCATCTCCCTCACTTAAGTCTCAGGCCTGTCA GCAGCTCCTGTGGACATTGCCATCCCCTCTGGTAGCCTTCAGAGCAAACAGGACAACCTATG TTATGGATGTTTCCACCAACCAGGGTAGTGGCATGGAGCACCGTAACCATCTGTGCTTCTGT GATCTCTATGACAGAGCCACTTCTCCACCTCTGAAATGTTCCCTGCTCTGAAATCTGGCATG GTCTGTTCTCTTATTGTCAACCTCAGCACAACAGGCTGGCGCCAATGGCATTACAGAGAAAG CAATCTGTGTGGCTAGTGGGCAGATTACCATGCAAGCCCCAGGAGAAATGGAGGAGCTTTGT AGCCACCTCCCTGTCAGCCAGTATTAACATGTCCCCTTCCCCCTGCCCCGCCGTAGATTCAG GACATTCGCCCTGTGTGCCACCAAACCAGGACTTTCCCCTTGGCTTGGCATCCCTGGCTCT CTCCTGGTACCCAGCAAGACGTCTGTTCCAGGGCAGTGTAGCATCTTTCAAGCTCCGTTACT ATGGCGATGGCCATGATGTTACAATCCCACTTGCCTGAATAATCAAGTGGGAAGGGGAAGCA GAGGGAAATGGGGCCATGTGAATGCAGCTGCTCTGTTCTCCCTACCCTGAGGAAAAACCAAA TGTTGAAGGGCACAAGAAATGTAGCTGGAGAAGATTGATGAAAGTGCAGGTGTGTAAGGAA ATAGAACAGTCTGCTGGGAGTCAGACCTGGAATTCTGATTCCAAACTCTTTATTACTTTGGG AAGTCACTCAGCCTCCCGTAGCCATCTCCAGGGTGACGGAACCCAGTGTATTACCTGCTGG AACCAAGGAAACTAACAATGTAGGTTACTAGTGAATACCCCAATGGTTTCTCCAATTATGCC CATGCCACCAAAACAATAAAACAAAATTCTCTAACACTGAAA

195/310 FIGURE 192

 ${\tt MWLPLGLLSLCLSPLPILSSPSLKSQACQQLLWTLPSPLVAFRANRTTYVMDVSTNQGSGME} \\ {\tt HRNHLCFCDLYDRATSPPLKCSLL}$

امر/ مرح المحادث المح

GGAGCGACGTCACCGCC ATG GCAGCCATCAAAGCTTTGATTAGTTTGTCCTTTGGAGGAGCAATCGGACTGATGTTTTTGATGCTTGGATGTGCCCTTCCAATATACAACAAATACTGGCCCCT CTTTGTTCTATTTTTTACATCCTTTCACCTATTCCATACTGCATAGCAAGAAGATTAGTGG GTCGTGTCAGCTTTTGGACTCCCTATTGTATTTGCCAGAGCACATCTGATTGAGTGGGGAGC TTGTGCACTTGTTCTCACAGGAAACACAGTCATCTTTGCAACTATACTAGGCTTTTTCTTGG TCAAATGGACTTCCTGTCATTTGTTGGCCATTCACGCACACAGGAGATGGGGCAGTTAATGC TGAATGGTATAGCAAGCCTCTTGGGGGTATTTTAGGTGCTCCCTTCTCACTTTTATTGTAAG CATACTATTTCACAGAGACTTGCTGAAGGATTAAAAGGATTTTCTCTTTTTGGAAAAGCTTG ACTGATTTCACACTTATCTATAGTATGCTTTTTTGTGGTGTCCTGCTGAATTTAAATATTTAT GTGTTTTTCCTGTTAGGTTGATTTTTTTTGGAATCAATATGCAATGTTAAACACTTTTTTAA TGTAATCATTTGCATTGGTTAGGAATTCAGAATTCCGCCGGCTCTATTACTGGTCAAGTACA TCTTTTCTCTTAAAATTATTTAGCCTCCATTATTACAAAAAATTATAAAAATAAGTTTTCAG TCAGTCAGGATGACATCACTCCCAATGTTATGCAGACATACAGACGGTTGGCATACGTTATA GACTGTATACTCAGTGCAAATATAGCTGCATTTATACCTCAGAGGGGCCAAGTGTTAATGCC CATGCCCTCCGTTAAGGGTTGTTGGTTTTACTGGTAGACAGATGTTTTGTGGATTGAAAATT ATTTTATGGAATTGCTACAGAGGAGTGCTTTTCTTCTCAATTGTTAGAAGAATTTATGTTAA TAGAGTGAGTTGCAATGTGGGAAGAATGACATTGAAATTCCAGTTTTTGAATCCTGTTTCT ATTTATAAGTGAAATTTGTGATCTCCTATCAACCTTTCATGTTTTACCCTGTTAAAATGGAC ATACATGGAACCACTACTGATGAGGGACAGTTGTATGTTTGCATCATATATGCCAGAAAACC TTCCTCTGCTTCCTCCTTTTGACTTATTTGGTATGTTGTATATATTACATAAAATAACTTTT CAAATATAGTTTAATAACACTTAGAAGTGTTTACTTACCTGGAAAATAATTGCTATGCCGTA CATTCAGAGTGCCCCCTCCCCTGCAAGGCCTTGCCATGATTAACAAGTAACTTGTTAGTCTT ACAGATAATTCATGCATTAACAGTTTAAGATTTAGACCATGGTAATAGTAGTTCTTATTCTC TAAGGTTATATCATATGTAATTTAAAAGTATTTTTAAGACAAGTTTCCTGTATACCTCTGAA CTGTTTTGATTTTGAGTTCATCATGATAGATCTGCTGTTTCCTTATAAAAGGCATTTGTTGT GTGAGTTAATGCAAAGTAGCCAAGTCCAGCTATATAGCAGCTTCAGAAACATACCTGACCAA AAAATTCCCAGTAACCAGGCATGATCAATTTATAGTGGTCGTTTACATCTAATAATTATCAG GACTTTTTTCAGGAGTGGGTTATAAAAACATTCAAGTTGGTCTGACAGTATTTTGTTAAGGA TATTTGTTTGTATGTTTATTCAGTATACTTACATAAAAATTATTTCGCCATCAGCCAAAACT CAGTAATCATGACAGCTGTCTGTTTTTTTTGAAGTTTATTTCTCAAGAAAATGGGAATAAA TTTGGGATTTGTTCAGCTTTTTTACTAAAGATGCCTAAAGCCACAGGTTTTATTGCCTAACT TAAGCCATGACTTTTAGATATGAGATGACGGGAAGCAGGACGAAATATCGGCGTGTGGCTGG AGCCTTCCCACTGGAGGCTGAAAGTGGCTTGTGGTATTATAATGTTCAGATTTCAAGAGGAA GGTGCAGGTACACATGAGTTAGAGAGCTGGTGAGACAGTTGGGAACTCTTTGTGCTTGTGAT $\tt CTACTGGACTTTTTTTTGCAGGAAGTGCATTCTCTGGTCCTTTCCCTATTTTCTGTTCTGGA$ TGTCAGTGCAGTGCACTGCTACTGTTTTATCCACTTGGCCACAGACTTTTTCTAACAGCTGC GTATTATTTCTATATACTAATTGCATTGGCAGCATTGTGTCTTTGACCTTGTATACTAGCTT GACATAGTGCTGTCTCTGATTTCTAGGCTAGTTACTTGAGATATGAATTTTCCATAGAATAT GCACTGATACAACATTACCATTCTTCTATGGAAAGAAAACTTTTGATGATGAAACAATAAAG ATTTTAAATATCTATTTTAAAAAAAAAA

~97/310 FIGURE 194

MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTDAM SNACKELAIFLTTGIVVSAFGLPIVFARAHLIEWGACALVLTGNTVIFATILGFFLVFGSND DFSWQQW

FIGURE 195A

CCCACGCGTCCGCCCACGCGTCCGCCCACGCGTCCGCCCACGCGTCCGCC CACGCGTCCGCCCACGCGTCCGGTGCAAGCTCGCGCGCACACTGCCTGGTGGAGGGAAGGA CCGCCGCCGCCGCAAAGCATGAGTGAGCCCGCTCTCTGCAGCTGCCCGGGGCGCGAATGG CAGGCTGTTTCCGCGGAGTAAAAGGTGGCGCCGGTCAGTGGTCGTTTCCAATGACGGACATT AACCAGACTGTCAGATCCTGGGGAGTCGCGAGCCCCGAGTTTGGAGTTTTTCCCCCCCACAA CGTCACAGTCCGAACTGCAGAGGGAAAGGAAGGCGGCAGGAAGGCGGAAGCTCCGGC GGGCTGCCTCGGAAACACAGAGGGGTCTTCTCTCGCCCTGCATATAATTAGCCTGCACACAA AGGGAGCAGCTGAATGGAGGTTGTCACTCTCTGGAAAAGGATTTCTGACCGAGCGCTTCCAA ${ t TGGACATTCTCCAGTCTCTGGAAAGATTCTCGCTA} { t ATG} { t GATTTCCTGCTGCTCGGTCTCT}$ CAGATGCTGCCCGCCCCCCAGCGGGTGCCCGCAGCTGTGCCGGTGCGAGGGGCGGCTGCT GTACTGCGAGGCGCTCAACCTCACCGAGGCGCCCCACAACCTGTCCGGCCTGCTGGGCTTGT CCCTGCGCTACAACAGCCTCTCGGAGCTGCGCGCCGGCCAGTTCACGGGGTTAATGCAGCTC ACGTGGCTCTATCTGGATCACAATCACATCTGCTCCGTGCAGGGGGACGCCTTTCAGAAACT GCGCCGAGTTAAGGAACTCACGCTGAGTTCCAACCAGATCACCCAACTGCCCAACACCCCT TCCGGCCCATGCCCAACCTGCGCAGCGTGGACCTCTCGTACAACAAGCTGCAGGCGCTCGCG CCCGACCTCTTCCACGGGCTGCGGAAGCTCACCACGCTGCATATGCGGGCCCAACGCCATCCA GTTTGTGCCCGTGCGCATCTTCCAGGACTGCCGCAGCCTCAAGTTTCTCGACATCGGATACA ATCAGCTCAAGAGTCTGGCGCGCAACTCTTTCGCCGGCTTGTTTAAGCTCACCGAGCTGCAC CTCGAGCACAACGACTTGGTCAAGGTGAACTTCGCCCACTTCCCGCGCCTCATCTCCCTGCA CTCGCTCTGCCTGCGGAGGAACAAGGTGGCCATTGTGGTCAGCTCGCTGGACTGGGTTTGGA ACCTGGAGAAAATGGACTTGTCGGGCAACGAGATCGAGTACATGGAGCCCCATGTGTTCGAG ACCGTGCCGCACCTGCAGTCCCTGCAGCTGGACTCCAACCGCCTCACCTACATCGAGCCCCG GATCCTCAACTCTTGGAAGTCCCTGACAAGCATCACCCTGGCCGGGAACCTGTGGGATTGCG GGCGCAACGTGTGCCCTAGCCTCGTGGCTCAGCAACTTCCAGGGGCGCTACGATGGCAAC TTGCAGTGCGCCAGCCCGGAGTACGCACAGGGCGAGGACGTCCTGGACGCCGTGTACGCCTT CCACCTGTGCGAGGATGGGGCCGAGCCCACCAGCGGCCACCTGCTCTCGGCCGTCACCAACC CACGACGGCACATTCGAGCCTGCCACCGTGGCTCTTCCAGGCGGCGAGCACGCCGAGAACGC CGTGCAGATCCACAAGGTGGTCACGGGCACCATGGCCCTCATCTTCTCCTCATCGTGG TTTGTCACGCAGCGCAGGAAGCAAAAGCAGAAACAGACCATGCATCAGATGGCTGCCATGTC TGCCCAGGAATACTACGTTGATTACAAACCGAACCACATTGAGGGAGCCCTGGTGATCATCA ${ t ACGAGTATGGCTCGTGTACCTGCCACCAGCAGCCCGCGAGGGAATGCGAGGTG}{ t TGTCC}$ CCAGGCTGGGGTCTCCTTGTCTGTGCTCTGATATGCTCCTTGACTGAAACTTTAAGGGGATC TCTCCCAGAGACTTGACATTTTAGCTTTATTGTGTCTTAAAAACAAAAGCGAATTAAAACAC AACAAAAAACCCCACCCCACAACCTTCAGGACAGTCTATCTTAAATTTCATATGAGAACTCC TTCCTCCCTTTGAAGATCTGTCCATATTCAGGAATCTGAGAGTGTAAAAAAGGTGGCCATAA GACAGAGAGAATAATCGTGCTTTGTTTTATGCTACTCCTCCCACCCTGCCCATGATTAAA CATCATGTATGTAGAAGATCTTAAGTCCATACGCATTTCATGAAGAACCATTGGAAAGAGGA ATCTGCAATCTGGGAGCTTAAGAGCAAATGATGACCATAGAAAGCTATGTTCTTACTTTGTG CGGGAATTTAGCTCACATCATTTCATGCCCCTGTGCCTCTAGCTCTGGAGATTGGTGGGGGG AGGTGGGGGGAAACGGCAGGAATAAGGGAAAGTGGTAGTTTTAACTAAGGTTTTGTAACACT TGAAATCTTTTCTTCTCAAATTAATTATCTTTAAGCTTCAAGAAACTTGCTCTGACCCCTC TATTCTTCCCACAGAGGGTGCTAATCTCATTATGCTGTGCTATCTGAAAAGAACTTAAGGCC ACAATTCACGTCTCGTCCTGGGCATTGTGATGGATTGACCCTCCATTTGCAGTACCTTCCCA GCTGATTAAAGTTCAGCAGTGGTATTGAGGTTTTTCGAATATTTATATAGAAAAAAAGTCTT TTCACATGACAAATGACACTCTCACACCAGTCTTAGCCCTAGTAGTTTTTTAGGTTGGACCA GAGGAAGCAGGTTAAATGAGACCTGTCCTCTGCTGCACTCAGAAAAAATAGGCAGTCCCTGA TGCTCAGATCTTAGCCTTGATATTAATAGTTGAGACCACCTACCCACAATGCAGCCTATACT CCCAAGACTACAAAGTTACCATCGCAAAGGAAAGGTTATTCCAGTAAAAGGAAATAGTTTTC TCAACCATTTAAAAATATTCTTCTGAACTCATCAAAGTAGAAGAGCCCCCAACCTTTTCTCT CTGCCTTCAAGAAGGCAGACATTTGGTATGATTTAGCATCAACAACACATTTATGAGTATAT

→ 38/310 FIGURE 195B

200/310 **FIGURE 196**

MDFLLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPH
NLSGLLGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNHICSVQGDAFQKLRRVKELTLSSNQ
ITQLPNTTFRPMPNLRSVDLSYNKLQALAPDLFHGLRKLTTLHMRANAIQFVPVRIFQDCRS
LKFLDIGYNQLKSLARNSFAGLFKLTELHLEHNDLVKVNFAHFPRLISLHSLCLRRNKVAIV
VSSLDWVWNLEKMDLSGNEIEYMEPHVFETVPHLQSLQLDSNRLTYIEPRILNSWKSLTSIT
LAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDAVYAFHLCEDGAEPTSG
HLLSAVTNRSDLGPPASSATTLADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMA
LIFSFLIVVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQMAAMSAQEYYVDYKPNH
IEGALVIINEYGSCTCHQQPARECEV

FIGURE 197

FIGURE 198

MGVLGRVLLWLQLCALTQAVSKLWVPNTDFDVAANWSQNRTPCAGGAVEFPADKMVSVLVQE GHAVSDMLLPLDGELVLASGAGFGVSDVGSHLDCGAGEPAVFRDSDRFSWHDPHLWRSGDEA PGLFFVDAERVPCRHDDVFFPPSASFRVGLGPGASPVRVRSISALGRTFTRDEDLAVFLASR AGRLRFHGPGALSVGPEDCADPSGCVCGNAEAQPWICAALLQP

FIGURE 199

FIGURE 200

 ${\tt MGPVKQLKRMFEPTRLIATIMVLLCFALTLCSAFWWHNKGLALIFCILQSLALTWYSLSFIP} \\ {\tt FARDAVKKCFAVCLA}$

FIGURE 201

TTGAGCGCAGGTGAGCTCCTGCGCGTTCCGGGGGCGTTCCTCCAGTCACCCTCCCGCCGTTA ACTACCATCCATAGCCAGATAGATTATCTTACACTGAACTGATCAAGTACTTTGAAAATGAC TTCGAAATTTATCTTGGTGTCCTTCATACTTGCTGCACTGAGTCTTTCAACCACCTTTTCTC TCCAACTAGACCAGCAAAAGGTTCTACTAGTTTCTTTTGATGGATTCCGTTGGGATTACTTA TATAAAGTTCCAACGCCCCATTTTCATTATATTATGAAATATGGTGTTCACGTGAAGCAAGT TACTAATGTTTTTATTACAAAAACCTACCCTAACCATTATACTTTGGTAACTGGCCTCTTTG CAGAGAATCATGGGATTGTTGCAAATGATATGTTTGATCCTATTCGGAACAAATCTTTCTCC TTGGATCACATGAATATTTATGATTCCAAGTTTTGGGAAGAAGCGACACCAATATGGATCAC AAACCAGAGGGCAGGACATACTAGTGGTGCAGCCATGTGGCCCGGAACAGATGTAAAAATAC ATAAGCGCTTTCCTACTCATTACATGCCTTACAATGAGTCAGTTTCATTTGAAGATAGAGTT GCCAAAATTGTTGAATGGTTTACGTCAAAAGAGCCCATAAATCTTGGTCTTCTCTATTGGGA AGACCCTGATGACATGGGCCACCATTTGGGACCTGACAGTCCGCTCATGGGGCCTGTCATTT CAGATATTGACAAGAAGTTAGGATATCTCATACAAATGCTGAAAAAGGCAAAGTTGTGGAAC ACTCTGAACCTAATCATCACAAGTGATCATGGAATGACGCAGTGCTCTGAGGAAAGGTTAAT CCATCTTGCCAAAAGAAGGTAAATTTGATGAAGTCTATGAAGCACTAACTCACGCTCATCCT AATCTTACTGTTTACAAAAAAGAAGACGTTCCAGAAAGGTGGCATTACAAATACAACAGTCG AATTCAACCAATCATAGCAGTGGCTGATGAAGGGTGGCACATTTTACAGAATAAGTCAGATG ACTTTCTGTTAGGCAACCACGGTTACGATAATGCGTTAGCAGATATGCATCCAATATTTTTA GCCCATGGTCCTGCCTTCAGAAAGAATTTCTCAAAAGAAGCCATGAACTCCACAGATTTGTA CCCACTACTATGCCACCTCCTCAATATCACTGCCATGCCACACAATGGATCATTCTGGAATG TCCAGGATCTGCTCAATTCAGCAATGCCAAGGGTGGTCCCTTATACACAGAGTACTATACTC CTCCCTGGTAGTGTTAAACCAGCAGAATATGACCAAGAGGGGTCATACCCTTATTTCATAGG GGTCTCTCTTGGCAGCATTATAGTGATTGTATTTTTTTGTAATTTTCATTAAGCATTTAATTC ACAGTCAAATACCTGCCTTACAAGATATGCATGCTGAAATAGCTCAACCATTATTACAAGCC $\underline{\textbf{TAA}} \textbf{TGTTACTTTGAAGTGGATTTGCATATTGAAGTGGAGATTCCATAATTATGTCAGTGTTT$ AAAGGTTTCAAATTCTGGGAAACCAGTTCCAAACATCTGCAGAAACCATTAAGCAGTTACAT AGATCCTGCTTTATTTGGACTTGGCGCAGATAATGTATATTTTAGCAACTTTGCACTATGT AAAGTACCTTATATATTGCACTTTAAATTTCTCTCTGATGGGTACTTTAATTTGAAATGCA CTTTATGGACAGTTATGTCTTATAACTTGATTGAAAATGACAACTTTTTTGCACCCATGTCAC AGAATACTTGTTACGCATTGTTCAAACTGAAGGAAATTTCTAATAATCCCGAATAATGAACA TAGAAATCTATCTCCATAAATTGAGAGAAGAAGAAGGTGATAAGTGTTGAAAATTAAATGTG ATAACCTTTGAACCTTGAATTTTGGAGATGTATTCCCAACAGCAGAATGCAACTGTGGGCAT AAATACTGACAGATTCGTTCTAAATATATTGTTTCTGTCATAAAATTATTGTGATTTCCTGA TGAGTCATATTACTGTGATTTTCATAATAATGAAGACACCATGAATATACTTTTCTTCTATA TAGTTCAGCAATGGCCTGAATAGAAGCAACCAGGCACCATCTCAGCAATGTTTTCTCTTGTT ΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑ

€06/310 FIGURE 202

MTSKFILVSFILAALSLSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVK
QVTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEEATPIW
ITNQRAGHTSGAAMWPGTDVKIHKRFPTHYMPYNESVSFEDRVAKIVEWFTSKEPINLGLLY
WEDPDDMGHHLGPDSPLMGPVISDIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEER
LIELDQYLDKDHYTLIDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYN
SRIQPIIAVADEGWHILQNKSDDFLLGNHGYDNALADMHPIFLAHGPAFRKNFSKEAMNSTD
LYPLLCHLLNITAMPHNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYF
IGVSLGSIIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

عوم المراكزة FIGURE 203

GGATTTTTGTGATCCGCGATTCGCTCCCACGGGCGGACCTTTGTAACTGCGGGAGGCCCAG AGAGAGGCCAAGCCCTTGCCTTGGGTCACACAGCCAAAGGAGGCAGAGCCAGAACTCACAA ${\tt CCAGATCCAGAGGCAACAGGGAC} {\tt CATG} {\tt GCCACCTGGGACGAAAAGGCAGTCACCCGCAGGGCC}$ AAGGTGGCTCCCGCTGAGAGGATGAGCAAGTTCTTAAGGCACTTCACGGTCGTGGGAGACGA CTACCATGCCTGGAACATCAACTACAAGAAATGGGAGAATGAAGAGGAGGAGGAGGAGGAGGAG AGCAGCCACCACCCACCCAGTCTCAGGCGAGGAAGGCAGAGCTGCAGCCCCTGACGTTGCC CCTGCCCCTGGCCCCGCACCCAGGGCCCCCTTGACTTCAGGGGCATGTTGAGGAAACTGTT CAGCTCCCACAGGTTTCAGGTCATCATCTGCTTGGTGGTTCTGGATGCCCTCCTGGTGC TTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCCGACAAGAATAACTATGCTGCCATG ATTTGTCTTCCGCCTGAGTTCTTTCACCACAAGTTTGAGATCCTGGATGCCCGTCGTGGTGG TGGTCTCATTCATCCTGGACATTGTCCTCCTGTTCCAGGAGCACCAGTTTGAGGCTCTGGGC $\tt CTGCTGATTCTGCTCCGGCTGTGGCGGGTGGCCCGGATCATCAATGGGATTATCATCTCAGT$ TAAGACACGTTCAGAACGGCAACTCTTAAGGTTAAAACAGATGAATGTACAATTGGCCGCCA ${\tt AGATTCAACACCTTGAGTTCAGCTGCTCTGAGAAGCCCCTGGAC\underline{\textbf{TGA}}\texttt{TGAGTTTGCTGTATC}$ AACCTGTAAGGAGAAGCTCTCTCCGGATGGCTATGGGAATGAAAGAATCCGACTTCTACTCT CACACAGCCACCGTGAAAGTCCTGGAGTAAAATGTGCTGTGTACAGAAGAGAGAAGAAGAAG CAGGCTGGCATGTTCACTGGGCTGTTTACGACAGAGAACCTGACAGTCACTGGCCAGTTA TCACTTCAGATTACAAATCACACAGAGCATCTGCCTGTTTTCAATCACAAGAGAACAAAACC AAAATCTATAAAGATATTCTGAAAATATGACAGAATTGACAAATAAAAGCATAAACGTGTA **ААААААААААААААААААААААААААААА**

५०४/७।० FIGURE 204

MATWDEKAVTRRAKVAPAERMSKFLRHFTVVGDDYHAWNINYKKWENEEEEEEEQPPPTPV
SGEEGRAAAPDVAPAPGPAPRAPLDFRGMLRKLFSSHRFQVIIICLVVLDALLVLAELILDL
KIIQPDKNNYAAMVFHYMSITILVFFMMEIIFKLFVFRLSSFTTSLRSWMPVVVVVSFILDI
VLLFQEHQFEALGLLILLRLWRVARIINGIIISVKTRSERQLLRLKQMNVQLAAKIQHLEFS
CSEKPLD

२०५ /३।० FIGURE 205

CGGCTCGAGCTCGAGCCGAATCGGCTCGAGGGGCAGTGGAGCACCCAGCAGCAGCCCAACAT **G**CTCTGTCTGTGCCTGTACGTGCCGGTCATCGGGGAAGCCCAGACCGAGTTCCAGTACTTTG AGTCGAAGGGGCTCCCTGCCGAGCTGAAGTCCATTTTCAAGCTCAGTGTCTTCATCCCCTCC CAGGAATTCTCCACCTACCGCCAGTGGAAGCAGAAAATTGTACAAGCTGGAGATAAGGACCT TGATGGGCAGCTAGACTTTGAAGAATTTGTCCATTATCTCCAAGATCATGAGAAGAAGCTGA GGCTGGTGTTTAAGATTTTGGACAAAAAGAATGATGGACGCATTGACGCGCAGGAGATCATG CATGGATAAAAACGGCACGATGACCATCGACTGGAACGAGTGGAGAGACTACCACCTCCTCC ACCCCGTGGAAAACATCCCCGAGATCATCCTCTACTGGAAGCATTCCACGATCTTTGATGTG GGTGAGAATCTAACGGTCCCGGATGAGTTCACAGTGGAGGAGAGGCAGACGGGGATGTGGTG GAGACACCTGGTGGCAGGAGGTGGGGCAGGGCCGTATCCAGAACCTGCACGGCCCCCTGG ACAGGCTCAAGGTGCTCATGCAGGTCCATGCCTCCCGCAGCAACAACATGGGCATCGTTGGT GGCTTCACTCAGATGATTCGAGAAGGAGGGCCAGGTCACTCTGGCGGGGCAATGGCATCAA CGTCCTCAAAATTGCCCCCGAATCAGCCATCAAATTCATGGCCTATGAGCAGATCAAGCGCC TTGTTGGTAGTGACCAGGAGACTCTGAGGATTCACGAGAGGCTTGTGGCAGGGTCCTTGGCA GGGGCCATCGCCCAGAGCAGCATCTACCCAATGGAGGTCCTGAAGACCCGGATGGCGCTGCG GAAGACAGGCCAGTACTCAGGAATGCTGGACTGCGCCAGGAGGATCCTGGCCAGAGAGGGGG TGGCCGCCTTCTACAAAGGCTATGTCCCCAACATGCTGGGCATCATCCCCTATGCCGGCATC GACCTTGCAGTCTACGAGACGCTCAAGAATGCCTGGCTGCAGCACTATGCAGTGAACAGCGC GGACCCCGCCTGTTTGTGCTCCTGGCCTGTGCACCATGTCCAGTACCTGTGGCCAGCTGG CCAGCTACCCCTGGCCCTAGTCAGGACCCGGATGCAGGCGCAAGCCTCTATTGAGGGCGCT CCGGAGGTGACCATGAGCAGCCTCTTCAAACATATCCTGCGGACCGAGGGGGCCTTCGGGCT GTACAGGGGGCTGGCCCCAACTTCATGAAGGTCATCCCAGCTGTGAGCATCAGCTACGTGG GCAGTGGACTCGCTGATCCTGGGCCGCAGCCTGGGGTGTGCAGCCATCTCATTCTGTGAATG GGGGAGAGCTGGCAGGCCCAGGGCTTGTCCTGCTGACCCCAGCAGACCCTCCTGTTGGTTCC AGCGAAGACCACAGGCATTCCTTAGGGTCCAGGGTCAGCAGGCTCCGGGCTCACATGTGTAA GGACAGGACATTTTCTGCAGTGCCTGCCAATAGTGAGCTTGGAGCCTGGAGGCCGGCTTAGT TCTTCCATTTCACCCTTGCAGCCAGCTGTTGGCCACGGCCCCTGCCCTCTGGTCTGCCGTGC ATCTCCCTGTGCCCTGCCTGCCTGTCTGCTGAGGTAAGGTGGGAGGAGGGCTACAG CCCACATCCCACCCCTCGTCCAATCCCATAATCCATGATGAAAGGTGAGGTCACGTGGCCT GATCTGGCCTTGTGGTCACTGGCATCTGAGCCCTGCTGATGGCTGGGGCTCTCGGGCATGCT ${\tt TGGGAGTGCAGGGGGCTCGGCTGGCTGGCTGCACAGAAGGCAAGTGCTGGGGCTCA}$ TGGTGCTCTGAGCTGGCCTGGACCCTGTCAGGATGGGCCCCACCTCAGAACCAAACTCACTG TCCCCACTGTGGCATGAGGGCAGTGGAGCACCATGTTTGAGGGCGAAGGGCAGAGCGTTTGT GTGTTCTGGGGAGGAAAAGGTGTTGGAGGCCTTAATTATGGACTGTTGGGAAAAGGG TTTTGTCCAGAAGGACAAGCCGGACAAATGAGCGACTTCTGTGCTTCCAGAGGAAGACGAGG GAGCAGGAGCTTGGCTGACTGCTCAGAGTCTGTTCTGACGCCCTGGGGGTTTCCTGTCCAACC CCAGCAGGGGCGCAGCCAGCCCCACATTCCACTTGTGTCACTGCTTGGAACCTATTT AAGCCCGCCCAGTGGGATGGGAGGAGGAGGAGGAGGGGGCCTTGGGCCGCTGCAGTCACAT CTGTCCAGAGAAATTCCTTTTGGGACTGGAGGCAGAAAAGCGGCCAGAAGGCAGCAGCCCTG GCTCCTTTCCTTTGGCAGGTTGGGGAAGGGCTTGCCCCCAGCCTTAGGATTTCAGGGTTTGA CTGGGGGCGTGGAGAGAGGGGGGAACCTCAATAACCTTGAAGGTGGAATCCAGTTATTTC CTGCGCTGCGAGGGTTTCTTTATTTCACTCTTTTCTGAATGTCAAGGCAGTGAGGTGCCTCT CAGCCTTCTGCTGCCTTGCTTAACAATGCCGGCCAACTGGCGACCTCACGGTTGCACTTCC ATTCCACCAGAATGACCTGATGAGGAAATCTTCAATAGGATGCAAAGATCAATGCAAAAATT

FIGURE 206

MLCLCLYVPVIGEAQTEFQYFESKGLPAELKSIFKLSVFIPSQEFSTYRQWKQKIVQAGDKD
LDGQLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEIMQSLRDLGVKISEQQAEKILK
SMDKNGTMTIDWNEWRDYHLLHPVENIPEIILYWKHSTIFDVGENLTVPDEFTVEERQTGMW
WRHLVAGGGAGAVSRTCTAPLDRLKVLMQVHASRSNNMGIVGGFTQMIREGGARSLWRGNGI
NVLKIAPESAIKFMAYEQIKRLVGSDQETLRIHERLVAGSLAGAIAQSSIYPMEVLKTRMAL
RKTGQYSGMLDCARRILAREGVAAFYKGYVPNMLGIIPYAGIDLAVYETLKNAWLQHYAVNS
ADPGVFVLLACGTMSSTCGQLASYPLALVRTRMQAQASIEGAPEVTMSSLFKHILRTEGAFG
LYRGLAPNFMKVIPAVSISYVVYENLKITLGVQSR

-211 /310 **FIGURE 207**

GGAAGGCAGCGGCAGCTCCACTCAGCCAGTACCCAGATACGCTGGGAACCTTCCCCAGCCAT CAATTGCACTCATCATTGGCTTTGGTATTTCAGGGAGACACTCCATCACAGTCACTACTGTC GCCTCAGCTGGGAACATTGGGGAGGATGGAATCCTGAGCTGCACTTTTGAACCTGACATCAA ACTTTCTGATATCGTGATACAATGGCTGAAGGAAGGTGTTTTAGGCTTGGTCCATGAGTTCA AAGAAGGCAAAGATGAGCTGTCGGAGCAGGATGAAATGTTCAGAGGCCGGACAGCAGTGTTT GCTGATCAAGTGATAGTTGGCAATGCCTCTTTGCGGCTGAAAAACGTGCAACTCACAGATGC TGGCACCTACAAATGTTATATCATCACTTCTAAAGGCAAGGGGAATGCTAACCTTGAGTATA AAACTGGAGCCTTCAGCATGCCGGAAGTGAATGTGGACTATAATGCCAGCTCAGAGACCTTG CGGTGTGAGGCTCCCCGATGGTTCCCCCAGCCCACAGTGGTCTGGGCATCCCAAGTTGACCA GGGAGCCAACTTCTCGGAAGTCTCCAATACCAGCTTTGAGCTGAACTCTGAGAATGTGACCA TGAAGGTTGTGTCTGTGCTCTACAATGTTACGATCAACAACACATACTCCTGTATGATTGAA AATGACATTGCCAAAGCAACAGGGGATATCAAAGTGACAGAATCGGAGATCAAAAGGCGGAG GGGCACTTCTGCCTCTCAGCCCTTACCTGATGCTAAAATAATGTGCCTTGGCCACAAAAAAG CATGCAAAGTCATTGTTACAACAGGGATCTACAGAACTATTTCACCACCAGATATGACCTAG TTTTATATTTCTGGGAGGAAATGAATTCATATCTAGAAGTCTGGAGTGAGCAAACAAGAGCA GACATATTAGAAGTTGGGAAAATAATTCATGTGAACTAGACAAGTGTGTTAAGAGTGATAAG GGGGAGTGAGAGGACAGGATAGTGCATGTTCTTTGTCTCTGAATTTTTAGTTATATGTGCTG TAATGTTGCTCTGAGGAAGCCCCTGGAAAGTCTATCCCAACATATCCACATCTTATATTCCA CAAATTAAGCTGTAGTATGTACCCTAAGACGCTGCTAATTGACTGCCACTTCGCAACTCAGG GGCGGCTGCATTTTAGTAATGGGTCAAATGATTCACTTTTTATGATGCTTCCAAAGGTGCCT TGGCTTCTCTCCCAACTGACAAATGCCAAAGTTGAGAAAAATGATCATAATTTTAGCATAA ACAGAGCAGTCGGGGACACCGATTTTATAAATAAACTGAGCACCTTCTTTTTAAACAAAAAA

=12/310 FIGURE 208

MASLGQILFWSIISIIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDI KLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASLRLKNVQLTD AGTYKCYIITSKGKGNANLEYKTGAFSMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVD QGANFSEVSNTSFELNSENVTMKVVSVLYNVTINNTYSCMIENDIAKATGDIKVTESEIKRR SHLQLLNSKASLCVSSFFAISWALLPLSPYLMLK

<13 /310 FIGURE 209

GAATTTGTAGAAGACAGCGGCGTTGCCATGGCGGCGTCTCTGGGGCAGGTGTTGGCTCTGGT GCTGGTGGCCGCTCTGTGGGGTGGCACGCAGCCGCTGCTGAAGCGGGCCTCCGCCGGCCTGC AGCGGGTTCATGAGCCGACCTGGGCCCAGCAGTTGCTACAGGAGATGAAGACCCTCTTCTTG AATACTGAGTACCTGATGCCCTTTCTCCTCAACCAGTGTGGATCCCTTCTCTATTACCTCAC CTTGGCATCGACAGATCTGACCCTGGCTGTGCCCATCTGTAACTCTCTGGCTATCATCTTCA CACTGATTGTTGGGAAGGCCCTTGGAGAAGATATTGGTGGAAAACGTAAGTTAGACTACTGC CTCCCAGAGTGGGTGAGGACACGGCCTTTTCCCATCCTGCCCTTTCCTCTGCAGCTGTTTT GCTTCCTTGTGGCCATCAGAGTTCCCTTCCCCTGGACAGTCTGGAGAAAGACAGAGGCTGGG GTTTGGGATTGAAGACCAGACCCCATCTGAGCCCTTCCTCCAGCCCTGTACCAGCTCCTACT GGCATGGCTGAGCTCAGACCCTCCTGATTTCTGCCTATTATCCCAGGAGCAGTTGCTGGCAT GGTGCTCACCGTGATAGGAATTTCACTCTGCATCACAAGCTCAGTGAGTAAGACCCAGGGGC AACAGTCTACCCTTTGAGTGGGCCGAACCCACTTCCAGCTCTGCTGCCTCCAGGAAGCCCCT GGGCCATGAAGTGCTGGCAGTGAGCGGATGGACCTAGCACTTCCCCTCTCTGGCCTTAGCTT CCTCCTCTTTATGGGGATAACAGCTACCTCATGGATCACAATAAGAGAACAAGAGTGAAAG AGTTTTGTAACCTTCAAGTGCTGTTCAGCTGCGGGGATTTAGCACAGGAGACTCTACGCTCA CCCTCAGCAACCTTTCTGCCCCAGCAGCTCTCTTCCTGCTAACATCTCAGGCTCCCAGCCCA GCCACCATTACTGTGGCCTGATCTGGACTATCATGGTGGCAGGTTCCATGGACTGCAGAACT CCAGCTGCATGGAAAGGGCCAGCTGCAGACTTTGAGCCAGAAATGCAAACGGGAGGCCTCTG GGACTCAGTCAGAGCGCTTTGGCTGAATGAGGGGTGGAACCGAGGGAAGAAGGTGCGTCGGA AAATCCTCACTGCCAGCCCCTCTTAAACAGGTAGAGAGCTGTGAGCCCCAGCCCCACCTGAC

214/310 FIGURE 210

MAASLGQVLALVLVAALWGGTQPLLKRASAGLQRVHEPTWAQQLLQEMKTLFLNTEYLMPFL LNQCGSLLYYLTLASTDLTLAVPICNSLAIIFTLIVGKALGEDIGGKRKLDYCECGTQLCGS RHTCVSSFPEPISPEWVRTRPFPILPFPLOLFCFLVAIRVPFPWTVWRKTEAGVWD

FIGURE 211

CTTCTGTAGGACAGTCACCAGGCCAGATCCAGAAGCCTCTCTAGGCTCCAGCTTTCTCTGTG GAAGATGACAGCAATTATAGCAGGACCCTGCCAGGCTGTCGAAAAGATTCCGCAATAAAACT TTGCCAGTGGGAAGTACCTAGTGAAACGGCCTAAGATGCCACTTCTTCTCATGTCCCAGGCT TGAGGCCCTGTGGTCCCCATCCTTGGGAGAAGTCAGCTCCAGCACCATGAAGGGCATCCTCG TTGCTGGTATCACTGCAGTGCTTGTTGCAGCTGTAGAATCTCTGAGCTGCGTGCAGTGTAAT TCATGGGAAAAATCCTGTGTCAACAGCATTGCCTCTGAATGTCCCTCACATGCCAACACCAG CTGTATCAGCTCCTCAGCCAGCTCCTCTCTAGAGACACCAGTCAGATTATACCAGAATATGT TCTGCTCAGCGGAGAACTGCAGTGAGGAGACACACATTACAGCCTTCACTGTCCACGTGTCT GCTGAAGAACACTTTCATTTTGTAAGCCAGTGCTGCCAAGGAAAGGAATGCAGCAACACCAG CGATGCCCTGGACCCTCCCCTGAAGAACGTGTCCAGCAACGCAGAGTGCCCTGCTTGTTATG AATCTAATGGAACTTCCTGTCGTGGGAAGCCCTGGAAATGCTATGAAGAAGAACAGTGTGTC TTTCTAGTTGCAGAACTTAAGAATGACATTGAGTCTAAGAGTCTCGTGCTGAAAGGCTGTTC CAACGTCAGTAACGCCACCTGTCAGTTCCTGTCTGGTGAAAACAAGACTCTTGGAGGAGTCA TCCCACACGTGGGCTCCAAAGCTTCCCTCTACCTCTTGGCCCTTGCCAGCCTCCTTCTTCG GGGACTGCCCTGAGGTCCTGGGGCTGCACTTTGCCCAGCACCCCATTTCTGCTTCTCTG AGGTCCAGAGCACCCCTGCGGTGCTGACACCCTCTTTCCCTGCTCTGCCCCGTTTAACTGC CCAGTAAGTGGGAGTCACAGGTCTCCAGGCAATGCCGACAGCTGCCTTGTTCTTCATTATTA

FIGURE 212

MKGILVAGITAVLVAAVESLSCVQCNSWEKSCVNSIASECPSHANTSCISSSASSSLETPVR LYQNMFCSAENCSEETHITAFTVHVSAEEHFHFVSQCCQGKECSNTSDALDPPLKNVSSNAE CPACYESNGTSCRGKPWKCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATCQFLSGENK TLGGVIFRKFECANVNSLTPTSAPTTSHNVGSKASLYLLALASLLLRGLLP

جمع/۲/٥١٥ FIGURE 213

ACCCAGACTCCGACCGAAATGCAGCGGGTCAGTTTACGCTTTGGGGGCCCCCATGACCCGCAG CTACCGGAGCACCGCCCGGACTGGTCTTCCCCGGAAGACAAGGATAATCCTAGAGGACGAGA ATGATGCCATGGCCGACGCCGACCGCCTGGCTGGACCAGCGGCTGCCGAGCTCTTGGCCGCC ACGGTGTCCACCGGCTTTAGCCGGTCGTCCGCCATTAACGAGGAGGATGGGTCTTCAGAAGA GGGGGTTGTGATTAATGCCGGAAAGGATAGCACCAGCAGAGAGCTTCCCAGTGCGACTCCCA ATACAGCGGGGAGTTCCAGCACGAGGTTTATAGCCAATAGTCAGGAGCCTGAAATCAGGCTG ACTTCAAGCCTGCCGCGCTCCCCCGGGAGGTCTACTGAGGACCTGCCAGGCTCGCAGGCCAC CCTGAGCCAGTGGTCCACACCTGGGTCTACCCCGAGCCGGTGGCCGTCACCCTCACCCACAG CCATGCCATCTCCTGAGGATCTGCGGCTGGTGCTGATGCCCTGGGGCCCGTGGCACTGCCAC TGCAAGTCGGGCACCATGAGCCGGAGCCGGTCTGGGAAGCTGCACGGCCTTTCCGGGCGCCCT TCGAGTTGGGGCGCTGAGCCAGCTCCGCACGGAGCACAAGCCTTGCACCTATCAACAATGTC CCTGCAACCGACTTCGGGAAGAGTGCCCCCTGGACACAAGTCTCTGTACTGACACCAACTGT GCCTCTCAGAGCACCACCAGTACCAGGACCACCACTACCCCCTTCCCCACCATCCACCTCAG AAGCAGTCCCAGCCTGCCACCCGCCAGCCCTGCCCAGCCCTGGCTTTTTGGAAACGGGTCA GGATTGGCCTGGAGGATATTTGGAATAGCCTCTCTTCAGTGTTCACAGAGATGCAACCAATA ${\tt GACAGAAACCAGAGG} \underline{{\tt TAA}} {\tt TGGCCACTTCATCCACATGAGGAGATGTCAGTATCTCAACCTCT}$ CTTGCCCTTTCAATCCTAGCACCCACTAGATATTTTTAGTACAGAAAAACAAAACTGGAAAA CACAA

حرا 8 /310 FIGURE 214

MVPAAGALLWVLLLNLGPRAAGAQGLTQTPTEMQRVSLRFGGPMTRSYRSTARTGLPRKTRI
ILEDENDAMADADRLAGPAAAELLAATVSTGFSRSSAINEEDGSSEEGVVINAGKDSTSREL
PSATPNTAGSSSTRFIANSQEPEIRLTSSLPRSPGRSTEDLPGSQATLSQWSTPGSTPSRWP
SPSPTAMPSPEDLRLVLMPWGPWHCHCKSGTMSRSRSGKLHGLSGRLRVGALSQLRTEHKPC
TYQQCPCNRLREECPLDTSLCTDTNCASQSTTSTRTTTTPFPTIHLRSSPSLPPASPCPALA
FWKRVRIGLEDIWNSLSSVFTEMQPIDRNQR

~19/310 FIGURE 215

CTAGCTGGGGCAGCGCCTGGCGAGCGGCTCCCAGGGCGACCGTGAGCCGGTGTACCGCGA CTGCGTACTGCAGTGCGAAGAGCAGAACTGCTCTGGGGGGCGCTCTGAATCACTTCCGCTCCC GCCAGCCAATCTACATGAGTCTAGCAGGCTGGACCTGTCGGGACGACTGTAAGTATGAGTGT ATGTGGGTCACCGTTGGGCTCTACCTCCAGGAAGGTCACAAAGTGCCTCAGTTCCATGGCAA GTGGCCCTTCTCCCGGTTCCTGTTCTTCAAGAGCCGGCATCGGCCGTGGCCTCGTTTCTCA ATGGCCTGGCCAGCCTGGTGATGCTCTGCCGCTACCGCACCTTCGTGCCAGCCTCCTCCCCC ATGTACCACACCTGTGTGGCCTTCGCCTGGGTGTCCCTCAATGCATGGTTCTGGTCCACAGT CTTCCACACCAGGGACACTGACCTCACAGAGAAAATGGACTACTTCTGTGCCTCCACTGTCA TCCTACACTCAATCTACCTGTGCTGCGTCAGGACCGTGGGGCTGCAGCACCCAGCTGTGGTC AGTGCCTTCCGGGCTCTCCTGCTGCTCATGCTGACCGTGCACGTCTCCTACCTGAGCCTCAT CCGCTTCGACTATGGCTACAACCTGGTGGCCAACGTGGCTATTGGCCTGGTCAACGTGGTGT GGTGGCTGGCCTGTGGAACCAGCGGCGCTGCCTCACGTGCGCAAGTGCGTGGTG GTGGTCTTGCTGCAGGGGCTGTCCCTGCTCGAGCTGCTTGACTTCCCACCGCTCTTCTG GGTCCTGGATGCCATGCCATCTGGCACATCAGCACCATCCCTGTCCACGTCCTCTTTTTCA GCTTTCTGGAAGATGACAGCCTGTACCTGCTGAAGGAATCAGAGGACAAGTTCAAGCTGGAC TGAAGACCTTGGAGCGAGTCTGCCCCAGTGGGGATCCTGCCCCGCCCTGCTGGCCTCCCTT CTCCCTCAACCCTTGAGATGATTTTCTCTTTTCAACTTCTTGAACTTGGACATGAAGGATG TGGGCCCAGAATCATGTGGCCAGCCCACCCCTGTTGGCCCTCACCAGCCTTGGAGTCTGTT CTAGGGAAGGCCTCCCAGCATCTGGGACTCGAGAGTGGGCAGCCCCTCTACCTCCTGGAGCT GAACTGGGGTGGAACTGAGTGTTCTTAGCTCTACCGGGAGGACAGCTGCCTGTTTCCTCC CCACCAGCCTCCCCCACATCCCCAGCTGCCTGGCTGGGTCCTGAAGCCCTCTGTCTACCT GGGAGACCAGGGCCTTAGGGATACAGGGGGTCCCCTTCTGTTACCACCCCCAC GCGATTCTCCCCATGGGATCTTGAGGGACCAAGCTGCTGGGATTGGGAAGGAGTTTCACCCT GACCGTTGCCCTAGCCAGGTTCCCAGGAGGCCTCACCATACTCCCTTTCAGGGCCAGGGCTC CAGCAAGCCCAGGGCAAGGATCCTGTGCTGCTGTCTGGTTGAGAGCCTGCCACCGTGTGTCG GAGCTCAGGCCTAGGTGCGCAGTGTGGAGACGGGTGTTGTCGGGGAAGAGGTGTGGCTTCAA AGTGTGTGTGCAGGGGTGGGTGTGTTAGCGTGGGTTAGGGGAACGTGTGTGCGCGTGCT GGTGGGCATGTGAGATGACTGCCGGTGAATGTCTCCACAGTTGAGAGGTTGGAGCAGG ATGAGGGAATCCTGTCACCATCAATAATCACTTGTGGAGCGCCAGCTCTGCCCAAGACGCCA CCTGGGCGGACAGCCAGGAGCTCTCCATGGCCAGGCTGCCTGTGTGCATGTTCCCTGTCTGG TGCCCCTTTGCCCGCCTCCTGCAAACCTCACAGGGTCCCCACACAACAGTGCCCTCCAGAAG CAGCCCTCGGAGGCAGAGGAAAATGGGGATGGCTGGGGCTCTCTCCATCCTCTTTT CTCCTTGCCTTCGCATGGCTGGCCTTCCCCTCCAAAACCTCCATTCCCCTGCTGCCAGCCCC TATGGCTGGGTCTGGTTTCTTCCCTTCCCAGAGGGTCTTACTGTTCCAGGGTGGCCCCAGGG CAGGCAGGGCCACACTATGCCTGTGCCCTGGTAAAGGTGACCCCTGCCATTTACCAGCAGC AGGCAGTCTCCGTGGTTGAAGCAGACTGGATTTTTGCTCTGCCCCTGACCCCTTGTCCCTCT TTGAGGGAGGGAGCTATGCTAGGACTCCAACCTCAGGGACTCGGGTGGCCTGCGCTAGCTT CTTTTGATACTGAAAACTTTTAAGGTGGGAGGGTGGCAAGGGATGTGCTTAATAAATCAATT CCAAGCCTCAAAAAAAAAAAAAAAAA

-20/210

FIGURE 216

MAGLAARLVLLAGAAALASGSQGDREPVYRDCVLQCEEQNCSGGALNHFRSRQPIYMSLAGW
TCRDDCKYECMWVTVGLYLQEGHKVPQFHGKWPFSRFLFFQEPASAVASFLNGLASLVMLCR
YRTFVPASSPMYHTCVAFAWVSLNAWFWSTVFHTRDTDLTEKMDYFCASTVILHSIYLCCVR
TVGLQHPAVVSAFRALLLLMLTVHVSYLSLIRFDYGYNLVANVAIGLVNVVWWLAWCLWNQR
RLPHVRKCVVVVLLLQGLSLLELLDFPPLFWVLDAHAIWHISTIPVHVLFFSFLEDDSLYLL
KESEDKFKLD

FIGURE 217

GGCCGCTGGAATTGTGGGAGTTGTCTCCCACTCGGCTGCCGGAGGCCGAAGGTCCGTGA CTATGCTCCCCAGAGCCTGCCTTCATCTAGGATGCTCCTCTGGGCATGCTGCTTGGGCTG CTGATGGCCGCCTGCTTCACCTTCTGCCTCAGTCATCAGAACCTGAAGGAGTTTGCCCTGAC TGGATGCCGAAGTCCTGGAGGTGTTCCACCCGACGCATGAGTGGCAGGCCCTTCAGCCAGGG CAGGCTGTCCCTGCAGGATCCCACGTACGGCTGAATCTTCAGACTGGGGAAAGAGAGGCAAA ACTCCAATATGAGGACAAGTTCCGAAATAATTTGAAAGGCAAAAGGCTGGATATCAACACCA ACACCTACACATCTCAGGATCTCAAGAGTGCACTGGCAAAATTCAAGGAGGGGGCAGAGATG GAGAGTTCAAAGGAAGACAAGGCAAGGCAGGCTGAGGTAAAGCGGCTCTTCCGCCCCATTGA GGAACTGAAGAAAGACTTTGATGAGCTGAATGTTGTCATTGAGACTGACATGCAGATCATGG TACGGCTGATCAACAAGTTCAATAGTTCCAGCTCCAGTTTGGAAGAGAAGATTGCTGCGCTC TTTGATCTTGAATATTATGTCCATCAGATGGACAATGCGCAGGACCTGCTTTCCTTTGGTGG TCTTCAAGTGGTGATCAATGGGCTGAACAGCACAGAGCCCCTCGTGAAGGAGTATGCTGCGT TTGTGCTGGGCGCTTTTCCAGCAACCCCAAGGTCCAGGTGGAGGCCATCGAAGGGGGA GCCCTGCAGAAGCTGCTGGTCATCCTGGCCACGGAGCAGCCGCTCACTGCAAAGAAGAAGAT CCTGTTTGCACTGTGCTCCCTGCTGCGCCACTTCCCCTATGCCCAGCGGCAGTTCCTGAAGC TCGGGGGGCTGCAGGTCCTGAGGACCCTGGTGCAGGAGAAGGGCACGGAGGTGCTCGCCGTG CGCGTGGTCACACTGCTCTACGACCTGGTCACGGAGAAGATGTTCGCCGAGGAGGAGGCTGA GCTGACCCAGGAGATGTCCCCAGAGAAGCTGCAGCAGTATCGCCAGGTACACCTCCTGCCAG GCCTGTGGGAACAGGGCTGGTGCGAGATCACGGCCCACCTCCTGGCGCTGCCCGAGCATGAT GCCCGTGAGAAGGTGCTGCAGACACTGGGCGTCCTCCTGACCACCTGCCGGGACCGCTACCG TCAGGACCCCCAGCTCGGCAGGACACTGGCCAGCCTGCAGGCTGAGTACCAGGTGCTGGCCA GCCTGGAGCTGCAGGATGGTGAGGACGAGGGCTACTTCCAGGAGCTGCTGGGCTCTGTCAAC AGCTTGCTGAAGGAGCTGAGA<u>TGA</u>GGCCCCACACCAGGACTGGACTGGGATGCCGCTAGTGA GGCTGAGGGGTGCCAGCGTGGGTGGGCTTCTCAGGCAGGAGGACATCTTGGCAGTGCTGGCT

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FIGURE 218

MAPQSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEEL
DAEVLEVFHPTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLKGKRLDINTN
TYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMV
RLINKFNSSSSSLEEKIAALFDLEYYVHQMDNAQDLLSFGGLQVVINGLNSTEPLVKEYAAF
VLGAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHFPYAQRQFLKL
GGLQVLRTLVQEKGTEVLAVRVVTLLYDLVTEKMFAEEEAELTQEMSPEKLQQYRQVHLLPG
LWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLGRTLASLQAEYQVLAS
LELODGEDEGYFQELLGSVNSLLKELR

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FIGURE 219

CTTCCCCGGGGTCTGGGGGTGACATTGCACCGCGCCCCTCGTGGGGTCGCGTTGCCACCCCA CGCGGACTCCCAGCTGGCGCGCCCCTCCCATTTGCCTGTCCTGGTCAGGCCCCCACCCCCC TTCCCACCTGACCAGCCATGGGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTCGCGTTCGGC CCGGCCTTCGCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGT CGCAGGGGCATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGG TCCATGTGACCGACCGGTCAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCT GTCTCTGTCCTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGA TGAAGGGTTAGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCT ATGTTTCTGGTCTCCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCT GATGCACTTGGGCCAGGTGTGGTTGGGATCCATGGAGACTCACCCTATTACTTCCTGACTTC AGCCTTTCTGACAGCCATTATCCTGCTCCATACCTTTTGGGGAGTTGTGTTCTTTGATG CCTGTGAGAGAGACGGTACTGGGCTTTGGGCCTGGTGGTTGGGAGTCACCTACTGACATCG GGACTGACATTCCTGAACCCCTGGTATGAGGCCAGCCTGCTGCCCATCTATGCAGTCACTGT TTCCATGGGGCTCTGGGCCTTCATCACAGCTGGAGGGTCCCTCCGAAGTATTCAGCGCAGCC CCCATGACTGAGCCCAGCCCCAGCCCGGGTCCATTGCCCACATTCTCTGTCTCCTTCTCGTC GGTCTACCCCACTACCTCCAGGGTTTTGCTTTGTCCTTTTGTGACCGTTAGTCTCTAAGCTT TACCAGGAGCAGCCTGGGTTCAGCCAGTCAGTGACTGGTGGGTTTGAATCTGCACTTATCCC CACCACCTGGGGACCCCCTTGTTGTGTCCAGGACTCCCCCTGTGTCAGTGCTCTGCTCTCAC CCTGCCCAAGACTCACCTCCCTTCCCCTCTGCAGGCCGACGCAGGAGGACAGTCGGGTGAT GGTGTATTCTGCCCTGCGCATCCCACCCGAGGACTGAGGGAACCTAGGGGGGACCCCTGGGC CTGGGGTGCCCTCTGATGTCCTCGCCCTGTATTTCTCCATCTCCAGTTCTGGACAGTGCAG GTTGCCAAGAAAAGGGACCTAGTTTAGCCATTGCCCTGGAGATGAAATTAATGGAGGCTCAA GGATAGATGAGCTCTGAGTTTCTCAGTACTCCCTCAAGACTGGACATCTTGGTCTTTTTCTC GAGGTGGGGGGGGGGGGGGTATATTGGAACTCTTCTAACCTCCTTGGGCTATATTTTCTC TCCTCGAGTTGCTCCTCATGGCTGGGCTCATTTCGGTCCCTTTCTCCTTGGTCCCAGACCTT GGGGGAAAGGAAGGAAGTGCATGTTTGGGAACTGGCATTACTGGAACTAATGGTTTTAACCT CCTTAACCACCAGCATCCCTCTCTCCCCAAGGTGAAGTGGAGGGTGCTGTGGTGAGCTGGC CACTCCAGAGCTGCAGTGCCACTGGAGGAGTCAGACTACCATGACATCGTAGGGAAGGAGGG ATCATTTTCTGCTGAGGGTGGAGTGTCCCATCCTTTTAATCAAGGTGATTGTGATTTTGACT ΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑΑ

FIGURE 220

MGAAVFFGCTFVAFGPAFALFLITVAGDPLRVIILVAGAFFWLVSLLLASVVWFILVHVTDR SDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVSGLS FGIISGVFSVINILADALGPGVVGIHGDSPYYFLTSAFLTAAIILLHTFWGVVFFDACERRR YWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRSLLCKD

جع /310 FIGURE 221

ન્સ્**5/**ઉ૧૦ **FIGURE 222**

GACCGACCGTTCAGATGCCCGGTTCCAGTACGGCTTCCTGATTTTTGGTGCTGCTGTNTCTG
TCCTTCTACAGGAGGTGTTCCGCTTTGCCTANTACAAGCTGCTTAAGAAGGCAGATGAGGGG
TTAGCATNGCTGAGTGAGGACGGAAGATCACCCATTTCCATCCGCCAGATGGCCTATGTTTN
TGGTNTTTCCTTCGGTATCATCAGTGGTGTTTTNTCTGTTATCAATATTTTGGNTGATGCAN
TTGGGCCAGGTGTGGTTGGGATCCATGGAGANTCACCCTATTAATTCCTGAATTCAGCCTTT
NTGACAGCAGCCATTATCCTGNTCCATACCTTTTGGGGAGTTGTTTTTTTGATGCCTGTGA
GAGGAG

FIGURE 223

NGTTGGAGAAGTGGCGCGGACNTTCATTTGGGGTTTCCCCCCTTTCCCCTTTCCCCG
GGGTCTGGGGTGACATTGCACGGGCCCCTCGTGGGGTCGCGTTGCCACCCCACGCGGACTCC
CCAGNTGGNGCGCCCTTCCCATTTGCCTGTCCTGGTCAGGCCCCCACCCCCCTTCCCACNTG
ACCAGCCATGGGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTCGCGTTCGGCCCGGCCTTCG
CGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGCA
TTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTTCATCTTTGGTCCATGTGAC
CGACCGGTCAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCTTCTCTCC
TTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTTA
GCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTGG
TCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTTG
GGCCAGGTGTGGTTGGGATCCATGGAGACTCACCC

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FIGURE 224

GTAAAAGAAAGTGGCCGGACCTTCATTGGGGTTTCGGTTCCCCCCTTTCCCNTTCCCCGGGG
TCTGGGGGTGACATTGCACCGCGCCCNTCGTGGGGTCGCGTTGCCACCCCACGCGGACTCCC
CAGNTGGCGCGCCCCTCCCATTTGCCTGTCCTGGTCAGGCCCCCACCCCCCTTCCCACCTGA
CCAGCCATGGGGGCTGCGGTGTTTTTCGGGCTGCACTTTCGTCGCGTTCGGGCCCGGCCTTC
GCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGC
ATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTTCATCTTGGTCCATGTGA
CCGACCGGTCAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTTGGTGCTGCTGTCTCTGTC
CTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTT
AGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTG
GTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTT
GGGCCAGGTGTGGTTTGGGATCCATGGAGAC

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FIGURE 225

GCCCAGGGAGCAGTGGTTATAACTCAGGCCCGGTGCCCAGAGCCCAGGAGGAGGCAG TGGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCCACCCCC TGTCTGTGCGTCCTGCACCCACATCTTTCTCTGTCCCCTCCTTGCCCTGTCTGGAGGCTGCT AGACTCCTATCTTCTGAATTCTATAGTGCCTGGGTCTCAGCGCAGTGCCGATGGTGGCCCGT CCTTGTGGTTCCTCTCTCTGGGGAAATAAGGTGCAGCGGCCATGCTACAGCAAGACCCC CCTGGATGTGGGTGCTCTGTGCTCTGATCACAGCCTTGCTTCTGGGGGTCACAGAGCATGTT CTCGCCAACATGATGTTTCCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCA GGACCTGGGAGCTGGGGCCGGGGAAGACGCCCGGTCGGATGACAGCAGCAGCCGCATCATCA ATGGATCCGACTGCGATATGCACACCCAGCCGTGGCAGGCCGCGCTGTTGCTAAGGCCCAAC CAGCTCTACTGCGGGGCGTGTTGGTGCATCCACAGTGGCTGCTCACGGCCGCCCACTGCAG GAAGAAGTTTTCAGAGTCCGTCTCGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGC AGCAGATGTTCCAGGGGGTCAAATCCATCCCCCACCTGGCTACTCCCACCCTGGCCACTCT AACGACCTCATGCTCATCAAACTGAACAGAAGAATTCGTCCCACTAAAGATGTCAGACCCAT CCAAGAGCCCCCAAGTGCACTTCCCTAAGGTCCTCCAGTGCTTGAATATCAGCGTGCTAAGT CAGAAAAGGTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGA ${\tt CAAAGCAGGTAGAGACTCCTGCCAGGGTGATTCTGGGGGGGCCTGTGGTCTGCAATGGCTCCC}$ TGCAGGGACTCGTGTCCTGGGGAGATTACCCTTGTGCCCGGCCCAACAGACCGGGTGTCTAC ACGAACCTCTGCAAGTTCACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCCTGAGTCAT CCCAGGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTTCAG ACCCTCATTCCTTCCCAGAGATGTTGAGAATGTTCATCTCTCCAGCCCCTGACCCCATGTCT CCTGGACTCAGGGTCTGCTTCCCCCACATTGGGCTGACCGTGTCTCTCTAGTTGAACCCTGG GAACAATTTCCAAAACTGTCCAGGGCGGGGGTTGCGTCTCAATCTCCCTGGGGCACTTTCAT CCTCAAGCTCAGGGCCCATCCCTTCTCTGCAGCTCTGACCCAAATTTAGTCCCAGAAATAAA CTGAGAAGTGGAAAAAAAA

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FIGURE 226

MATARPPWMWVLCALITALLLGVTEHVLANNDVSCDHPSNTVPSGSNQDLGAGAGEDARSDD SSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHYSLS PVYESGQQMFQGVKSIPHPGYSHPGHSNDLMLIKLNRRIRPTKDVRPINVSSHCPSAGTKCL VSGWGTTKSPQVHFPKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGDKAGRDSCQGDSGGP VVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

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FIGURE 227

ATGGTCAACGACCGGTGGAAGACCATGGGCGGCGCTGCCCAACTTGAGGACCGGCCGCGCGA CAAGCCGCAGCGGCCGAGCTGCGGCTACGTGCTGCACCGTGCTGCTGCCTGGCCTGTGC TGCTGGCTGTAGCTGTCACCGGTGCCGTGCTCTTCCTGAACCACGCCCACGCGCCGGGCACG GCGCCCCACCTGTCGTCAGCACTGGGGCTGCCAGCGCCCAACAGCGCCCTGGTCACTGTGGA AAGGGCGGACACCTCACCATCCTCATTGACCCGCGCTGCCCCGACCTCACCGACA GCTTCGCACGCCTGGAGAGCGCCCAGGCCTCGGTGCTGCAGGCGCTGACAGAGCACCAGGCC CAGCCACGGCTGGCGACCAGGAGCAGGAGCTGCTGGACACGCTGGCCGACCAGCTGCC CCGGCTGCTGGCCCGAGCCTCAGAGCTGCAGACGGAGTGCATGGGGCTGCGGAAGGGGCATG GCACGCTGGGCCAGGGCCTCAGCGCCCTGCAGAGTGAGCAGGGCCGCCTCATCCAGCTTCTC TCTGAGAGCCAGGGCCACATGGCTCACCTGGTGAACTCCGTCAGCGACATCCTGGATGCCCT GCAGAGGGACCGGGGCTGGGCCCGGCAACAAGGCCGACCTTCAGAGAGCGCCTGCCC GGGGAACCCGGCCCCGGGCTGTGCCACTGGCTCCCGGCCCCGAGACTGTCTGGACGTCCTC CCAGGTGTACTGTGACATGCGCACGGACGGCGGCGGCTGGACGGTGTTTCAGCGCCCGGGAGG ACGGCTCCGTGAACTTCTTCCGGGGCTGGGACGCGTACCGAGACGGCTTTGGCAGGCTCACC GGGGAGCACTGGCTAGGGCTCAAGAGGATCCACGCCCTGACCACACAGGCTGCCTACGAGCT GCACGTGGACCTGGAGGACTTTGAGAATGGCACGGCCTATGCCCGCTACGGGAGCTTCGGCG TGGGCTTGTTCTCCGTGGACCCTGAGGAAGACGGGTACCCGCTCACCGTGGCTGACTATTCC GGCACTGCAGGCGACTCCCTCCTGAAGCACAGCGCCATGAGGTTCACCACCAAGGACCGTGA CAGCGACCATTCAGAGAACAACTGTGCCGCCTTCTACCGCGGTGCCTGGTGGTACCGCAACT GCCACACGTCCAACCTCAATGGGCAGTACCTGCGCGGTGCGCACGCCTCCTATGCCGACGGC CCACTCTCCAGTAGGGAGGGCCGGGCCATCCCTGACACGAAGCTCCCTGGGCCGGTGAAGT CACACATCGCCTTCTCGCCGTCCCCACCCCCTCCATTTGGCAGCTCACTGATCTCTTGCCTC TGCTGTTTGCCGTCCCCTGGCCAGGATGGTGGAGTCTGCCCCAGGCACCCTCTGCCCTGCCC GGCCAAATACCCGGCATTATGGGGACAGAGAGCAGGGGGGGCAGACAGCACCCCTGGAGTCCTC CTAGCAGATCGTGGGGAATGTCAGGTCTCTCTGAGGTCAGGTCTGAGGCCAGTATCCTCCAG CCCTCCCAATGCCAACCCCCACCCCGTTTCCCTGGTGCCCAGAGAACCCACCTCTCCCCCAA GGGCCTCAGCCTGGGCTGGGCTGGGCCCCATCCTACCAGGCCCTGAGGTCAGGATGGG TCTCAAATGAGGCCCAACCCATCCCCCACCCAGCTCCCGGCCGTCCTCCTACCTGGGGCAGC GGACTGCGCTAATGGGAAGCTCTTGGTTTTCTGGGCTGGGGCCTAGGCAGGGCTGGGATGAG GCTTGTACAACCCCCACCAATTTCCCAGGGACTCCAGGGTCCTGAGGCCTCCCAGGAGG GCCTTGGGGGTGATGACCCCTTCCCTGAGGTGGCTGTCTCCATGAGGAGGCCAACCCTTGCC ATTGACCGTGGCCACCTGGACCCAGGCCAGGCCCGGCCGAGTGGTCAAGGGACAGGGA CCACCTCACCGGGCAAATGGGGTCGGGGGGACTGGGGCACCAGGCACCACCTGGACA CTTTCTTGTTGAATCCTCCCAACACCCAGCACGCTGTCATCCCCACTCCTTGTGTGCACACA TGCAGAGGTGAGACCCGCAGGCTCCCAGGACCAGCCACCAAGGGCAGGGCTGGAGCCGGG CGGCTTTTCCAAGGCCTCCTGATGGGGGCCTCCGAAAGGGCTGGAGTCAGCCTTGGGGAGCT GCCTAGCAGCCTCTCCTCGGGCAGGAGGGGGGGGGGGGTGGCTTCCTCCAAAGGACACCCGATGGCA GGTGCCTAGGGGGTGTGGGGTTCCGTTCTCCCTTCCCCTCCCACTGAAGTTTGTGCTTAAAA AACAATAAATTTGACTTGGCACCACTGGGGGTTGGTGGGAGAGGCCGTGTGACCTGGCTCTC TGTCCCAGTGCCACCAGGTCATCCACATGCGCAG

FIGURE 228

MVNDRWKTMGGAAQLEDRPRDKPQRPSCGYVLCTVLLALAVLLAVAVTGAVLFLNHAHAPGT
APPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALTEHQA
QPRLVGDQEQELLDTLADQLPRLLARASELQTECMGLRKGHGTLGQGLSALQSEQGRLIQLL
SESQGHMAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVL
LSGQQDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLT
GEHWLGLKRIHALTTQAAYELHVDLEDFENGTAYARYGSFGVGLFSVDPEEDGYPLTVADYS
GTAGDSLLKHSGMRFTTKDRDSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASYADG
VEWSSWTGWQYSLKFSEMKIRPVREDR

FIGURE 229

GCAGTCAGAGACTTCCCCTGCCCCTCGCTGGGAAAGAACATTAGGAATGCCTTTTAGTGCCT TGCTTCCTGAACTAGCTCACAGTAGCCCGGCGCCCAGGGCAATCCGACCACATTTCACTCT CACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGCTGGATGATG ATGGGGACACCACCATGAGCCTGCATTCTCAAGCCTCTGCCACAACTCGGCATCCAGAGCCC CGGCGCACAGAGCACAGGGCTCCCTCTTCAACGTGGCGACCAGTGGCCCTGACCCTGCTGAC ${\tt TTTGTGCTTGGTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTCAGTACTACC}$ CAAGAGTTGCAATCTCTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTCTGCAGCATGTGGC TGAAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGCACACAGGTGCAGCCCTTGTACAG AACAATGGAAATGGCATGGAGACAATTGCTACCAGTTCTATAAAGACAGCAAAAGTTGGGAG CCTGGAATTTGCCGCGTCTCAGAGCTACTCTGAGTTTTTCTACTCTTATTGGACAGGGCTTT TGCGCCCTGACAGTGGCAAGGCCTGGCTGTGGATGGAACCCCTTTCACTTCTGAACTG TTCCATATTATAATAGATGTCACCAGCCCAAGAAGCAGAGACTGTGTGGCCATCCTCAATGG TGGTGAAGCCAGAGAGCCTCCATGTCCCCCCTGAAACATTAGGCGAAGGTGACTGATTCGCC CTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAAGCAAGGGCTAGTTGAGACAT TGGGAAATGGAACATAATCAGGAAAGACTATCTCTCTGACTAGTACAAAATGGGTTCTCGTG TTTCCTGTTCAGGATCACCAGCATTTCTGAGCTTGGGTTTATGCACGTATTTAACAGTCACA AGAAGTCTTATTTACATGCCACCAACCAACCTCAGAAACCCATAATGTCATCTGCCTTCTTG GCTTAGAGATAACTTTTAGCTCTCTTTCTCTCAATGTCTAATATCACCTCCCTGTTTTCAT GTCTTCCTTACACTTGGTGGAATAAGAAACTTTTTGAAGTAGAGGAAATACATTGAGGTAAC ATCCTTTTCTCTGACAGTCAAGTAGTCCATCAGAAATTGGCAGTCACTTCCCAGATTGTACC AGCAAATACACAAGGAATTCTTTTTGTTTGTTTCAGTTCATACTAGTCCCTTCCCAATCCAT CAGTAAAGACCCCATCTGCCTTGTCCATGCCGTTTCCCAACAGGGATGTCACTTGATATGAG AATCTCAAATCTCAATGCCTTATAAGCATTCCTTCCTGTGTCCATTAAGACTCTGATAATTG TCTCCCCTCCATAGGAATTTCTCCCAGGAAAGAATATATCCCCATCTCCGTTTCATATCAG AACTACCGTCCCCGATATTCCCTTCAGAGAGATTAAAGACCAGAAAAAAGTGAGCCTCTTCA TCTGCACCTGTAATAGTTTCAGTTCCTATTTTCTTCCATTGACCCATATTTATACCTTTCAG GTACTGAAGATTTAATAATAATAATGTAAATACTGTGAAAAA

FIGURE 230

MQAKYSSTRDMLDDDGDTTMSLHSQASATTRHPEPRRTEHRAPSSTWRPVALTLLTLCLVLL
IGLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRE
LYNKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAAS
QSYSEFFYSYWTGLLRPDSGKAWLWMDGTPFTSELFHIIIDVTSPRSRDCVAILNGMIFSKD
CKELKRCVCERRAGMVKPESLHVPPETLGEGD

FIGURE 231

FIGURE 232

GCCGAGCGCAAGAACCCTGCGCAGCCCAGAGCAGCTGCTGGAGGGGAATCGAGGCGCGGCTC CGGGGATTCGGCTCGGGCTCTGCTCTGCGGGGAGGGAGCGGCCCGCCGCGGGG ${\tt TCGGTGCTGCGCCCGCAGGGCCCGTGGCCATCTCCCTGGGCTTCACCCTGAGCCT}$ GCTCAGCGTCACCTGGGTGGAGGAGCCGTGCGGCCCAGGCCCCCAACCTGGAGACTCTG AGCTGCCGCCGCGCCAACACCCAACGCGGCGCGCCCCAACTCGGTGCAGCCCGGAGCG GAGCGCGAGAAGCCCGGGGGCCGAAGGCGCCGGGGAGAATTGGGAGCCGCGCGTCTTGCC CTACCACCCTGCACAGCCCGGCCAGGCCGCCAAAAAGGCCGTCAGGACCCGCTACATCAGCA CGGAGCTGGGCATCAGGCAGAGGCTGCTGGTGGCGGTGCTGACCTCTCAGACCACGCTGCCC ACGCTGGGCGTGGAACCGCACGCTGGGGCACCGGCTGGAGCGTGTGGTGTTCCTGAC ${\tt CCATTGGACACCTGCGCGCTGCGCCACCTGCTGGAGCACGGCGACGACTTTGAC}$ TGGTTCTTCCTGGTGCCTGACACCACCTACACCGAGGCGCACGGCCTGGCACGCCTAACTGG GAGAGCCCACCCCGGCCGCTACTGCCACGGAGGCTTTGGGGTGCTGCTGTCGCGCATGCTG CTGCAACAACTGCGCCCCCACCTGGAAGGCTGCCGCAACGACATCGTCAGTGCGCGCCCTGA GGGTGCACTATAGCCATCTGGAGCTGAGCCCTGGGGAGCCAGTGCAGGAGGGGGACCCTCAT ${\tt TTCCGAAGTGCCCTGACAGCCCACCCTGTGCGTGACCCTGTGCACATGTACCAGCTGCACAA}$ AGCTTTCGCCCGAGCTGAACTGGAACGCACGTACCAGGAGATCCAGGAGTTACAGTGGGAGA TCCAGAATACCAGCCATCTGGCCGTTGATGGGGACCGGGCAGCTGCTTGGCCCGTGGGTATT CCAGCACCATCCCGCCCGGCCTCCCGCTTTGAGGTGCTGCGCTGGGACTACTTCACGGAGCA GCACGCTTTCTCCTGCGCCGATGGCTCACCCCGCTGCCCACTGCGTGGGGCTGACCGGGCTG ATGTGGCCGATGTTCTGGGGACAGCTCTAGAGGAGCTGAACCGCCGCCTACCACCCGGCCTTG ${\tt CGGCTCCAGAAGCAGCAGCTGGTGAATGGCTACCGACGCTTTGATCCGGCCCGGGGTATGGA}$ ATACACGCTGGACTTGCAGCTGGAGGCACTGACCCCCCAGGGAGGCCGCCGGCCCCTCACTC GCCGAGTGCAGCTGCTCCGGCCGCTGAGCCGCGTGGAGATCTTGCCTGTGCCCTATGTCACT GAGGCCTCACGTCTCACTGTGCTGCTGCCTCTAGCTGCGGCTGAGCGTGACCTGGCCCCTGG TGCTGCTACTGTATGAGCCGCGCCAGGCCCAGCGCGTGGCCCATGCAGATGTCTTCGCACCT GTCAAGGCCCACGTGGCAGAGCTGGAGCGGCGTTTCCCCGGGTGCCCGGGTGCCATGGCTCAG TGTGCAGACAGCCGCACCCTCACCACTGCGCCTCATGGATCTACTCTCCAAGAAGCACCCGC TGGACACACTGTTCCTGCTGGCCGGGCCAGACACGGTGCTCACGCCTGACTTCCTGAACCGC TGCCGCATGCATGCCATCTCCGGCTGGCAGGCCTTCTTTCCCATGCATTTCCAAGCCTTCCA CCCAGGTGTGGCCCCACCACAAGGGCCTGGGCCCCCAGAGCTGGGCCGTGACACTGGCCGCT TTGATCGCCAGGCAGCCAGCGAGGCCTGCTTCTACAACTCCGACTACGTGGCAGCCCGTGGG ACCGGGCCCAGACGTGCAGCGCGAGGCTCAGTGAGGACCTGTACCACCGCTGCCTCCAGAGC GTGCTTGAGGGCCTCGGCTCCCGAACCCAGCTGGCCATGCTACTCTTTGAACAGGAGCAGGG ${\tt CAACAGCACC} \underline{{\tt TGA}} {\tt CCCCACCCTGTCCCCGTGGGCCTGGCCATGGCCACCCCACCCCACTT}$ CTCCCCAAAACCAGAGCCACCTGCCAGCCTCGCTGGGCAGGGCTGGCCGTAGCCAGACCCC ${\tt AAGCTGGCCCACTGGTCCCTCTCTGGCTCTGTGGGTCCCTGGGCTCTGGACAAGCACTGGG}$ GGACGTGCCCCAGAGCCACCCACTTCTCATCCCAAACCCAGTTTCCCTGCCCCCTGACGCT GCTGATTCGGGCTGTGGCCTCCACGTATTTATGCAGTACAGTCTGCCTGACGCCAGCCCTGC GCATCTCCCAACTTCTCCCTTTTGGACCCTGCCGAAGCTCCCTGCCTTTAATAAACTGGCCA AGTGTGGAAAAA

FIGURE 233

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNAARRP
NSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAAKKAVRTRYISTELGIRQRLLVAVL
TSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEERPIGHLHLALRHLLE
QHGDDFDWFFLVPDTTYTEAHGLARLTGHLSLASAAHLYLGRPQDFIGGEPTPGRYCHGGFG
VLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGRCILDATGVGCTGDHEGVHYSHLELSPGEP
VQEGDPHFRSALTAHPVRDPVHMYQLHKAFARAELERTYQEIQELQWEIQNTSHLAVDGDRA
AAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSCADGSPRCPLRGADRADVADVLGTALEELN
RRYHPALRLQKQQLVNGYRRFDPARGMEYTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEI
LPVPYVTEASRLTVLLPLAAAERDLAPGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVA
HADVFAPVKAHVAELERRFPGARVPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTVL
TPDFLNRCRMHAISGWQAFFPMHFQAFHPGVAPPQGPGPPELGRDTGRFDRQAASEACFYNS
DYVAARGRLAAASEQEEELLESLDVYELFLHFSSLHVLRAVEPALLQRYRAQTCSARLSEDL
YHRCLQSVLEGLGSRTQLAMLLFEQEQGNST

FIGURE 234

GCTCTGGCCGGCCCGGCGATTGGTCACCGCCCGCTAGGGGACAGCCCTGGCCTCCTCTGAT TGGCAAGCGCTGGCCACCCCCACACCCCTTGCGAACGCTCCCCTAGTGGAGAAAAGGAGT AGCTATTAGCCAATTCGGCAGGGCCCGCTTTTTAGAAGCTTGATTTCCTTTGAAGATGAAAG ACTAGCGGAAGCTCTGCCTCTTTCCCCAGTGGGCGAGGGAACTCGGGGCGATTGGCTGGGAA CTGTATCCACCCAAATGTCACCGATTTCTTCCTATGCAGGAAATGAGCAGACCCATCAATAA GAAATTTCTCAGCCTGGCCGAAAATGGTTGGCCCCACGAAGCCCACGACAACTGGAGGCAAAG AGGGTTGCTCAACGCCCCGCCTCATTGGAAAACCAAATCAGATCTGGGACCTATATAGCGTG GCGGAGGCGGGCGATGATTGTCGCGCTCGCACCCACTGCAGCTGCGCACAGTCGCATTTCT ${\tt TTCCCCGCCCTGAGACCCTGCAGCACCATCTGTC} \underline{{\tt ATG}} {\tt GCGGCTGGGCTGTTTGGTTTGAGC}$ ATCTAGCTTCTCCAGGACTGTGGTCGCCCGTCCGCTGTGGCGGGAAAGCGGCCCCCAGAAC CGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGACGAAAACTTGTATGAGAAGAACCCA $\tt CTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACCTTTGTGGCCTATCTGCCTGACTACA$ GGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCCTTGTGAAATACCGAGAGGCCAATGGC $\tt CTTCCCATCATGGAATCCAACTGCTTCGACCCCAGCAAGATCCAGCTGCCAGAGGATGAG\underline{\textbf{TG}}$ CTCTTCTCAGAGCACCTAATTAAAGGGGCTGAAAGTCTGAA

FIGURE 235

MAAGLFGLSARRLLAAAATRGLPAARVRWESSFSRTVVAPSAVAGKRPPEPTTPWQEDPEPE DENLYEKNPDSHGYDKDPVLDVWNMRLVFFFGVSIILVLGSTFVAYLPDYRMKEWSRREAER LVKYREANGLPIMESNCFDPSKIQLPEDE

FIGURE 236

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TGCAGAACCCCCACGCGACAGCCTGCGGGGGGAGCTTGTCATCACCCCGCTGCCTTCCGGGG ACGTAGCCGCCACATTCCAGTTCCGCACGCGCTGGGATTCGGAGCTTCAGCGGGAAGGAGTG ${\tt TCCCATTACAGGCTCTTTCCCAAAGCCCTGGGGCAGCTGATCTCCAAGTATTCTCTACGGGA}$ ${\tt GCTGCACCTGTCATTCACACAAGGCTTTTGGAGGACCCGATACTGGGGGCCACCCTTCCTGC}$ AGGCCCCATCAGGTGCAGAGCTGTGGGTCTGGTTCCAAGACACTGTCACTGATGTGGATAAA TCTTGGAAGGAGCTCAGTAATGTCCTCTCAGGGATCTTCTGCGCCTCTCTCAACTTCATCGA CTCCACCAACACAGTCACTCCCACTGCCTCCTTCAAACCCCTGGGTCTGGCCAATGACACTG ACCACTACTTTCTGCGCTATGCTGTGCTGCCGCGGGAGGTGGTCTGCACCGAAAACCTCACC CCCTGGAAGAAGCTCTTGCCCTGTAGTTCCAAGGCAGGCCTCTCTGTGCTGCTGAAGGCAGA ${\tt TCGCTTGTTCCACACCAGCTACCACTCCCAGGCAGTGCATATCCGCCCTGTTTGCAGAAATG}$ ${\tt CACGCTGTACTAGCATCTCCTGGGAGCTGAGGCAGACCCTGTCAGTTGTATTTGATGCCTTC}$ ${\tt ATCACGGGGCAGGGAAAGAAGACTGGTCCCTCTTCCGGATGTTCTCCCGAACCCTCACGGA}$ GCCCTGCCCCTGGCTTCAGAGAGCCGAGTCTATGTGGACATCACCACCTACAACCAGGACA ACGAGACATTAGAGGTGCACCCACCCCGACCACTACATATCAGGACGTCATCCTAGGCACT CGGAAGACCTATGCCATCTATGACTTGCTTGACACCGCCATGATCAACAACTCTCGAAACCT CAACATCCAGCTCAAGTGGAAGAGACCCCCAGAGAATGAGGCCCCCCAGTGCCCTTCCTGC ATGCCCAGCGGTACGTGAGTGGCTATGGGCTGCAGAAGGGGGAGCTGAGCACACTGCTGTAC AACACCCACCCATACCGGGCCTTCCCGGTGCTGCTGCTGGACACCGTACCCTGGTATCTGCG GCTGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAACAAACCAAGTTACATCC ACTACCAGCCTGCCAGGACCGGCTGCAACCCCACCTCCTGGAGATGCTGATTCAGCTGCCG GCCAACTCAGTCACCAAGGTTTCCATCCAGTTTGAGCGGGCGCTGCTGAAGTGGACCGAGTA CACGCCAGATCCTAACCATGGCTTCTATGTCAGCCCCATCTGTCCTCAGCGCCCCTTGTGCCCA GCATGGTAGCAGCCAAGCCAGTGGACTGGGAAGAGAGTCCCCTCTTCAACAGCCTGTTCCCA GTCTCTGATGGCTCTAACTACTTTGTGCGGCTCTACACGGAGCCGCTGCTGGTGAACCTGCC GACACCGGACTTCAGCATGCCCTACAACGTGATCTGCCTCACGTGCACTGTGGTGGCCGTGT GCTACGGCTCCTTCTACAATCTCCTCACCCGAACCTTCCACATCGAGGAGCCCCGCACAGGT ${\tt GGCCTGGCCAAGCGTGGCCAACCTTATCCGGCGCGCCCGAGGTGTCCCCCCACTC} {\color{red}{\bf TGA}} {\tt TT}$ $\tt CTTGCCCTTTCCAGCAGCTGCAGCTGCCGTTTCTCTCTGGGGAGGGGAGCCCAAGGGCTGTT$ CTACAGCTGTGTTGTCCAGTACAGGAGCCACGAGCCAAATGTGGCATTTGAATTTAA CTTAGAAATTCATTTCCTCACCTGTAGTGGCCACCTCTATATTGAGGTGCTCAATAAGCAAA AGTGGTCGGTGGCTGCTATTGGACAGCACAGAAAAAGATTTCCATCACCACAGAAAGGTC GGCTGGCAGCACTGGCCAAGGTGATGGGGTGTGCTACACAGTGTATGTCACTGTGTAGTGGA

FIGURE 238

MPLALLVLLLGPGGWCLAEPPRDSLREELVITPLPSGDVAATFQFRTRWDSELQREGVSHY
RLFPKALGQLISKYSLRELHLSFTQGFWRTRYWGPPFLQAPSGAELWVWFQDTVTDVDKSWK
ELSNVLSGIFCASLNFIDSTNTVTPTASFKPLGLANDTDHYFLRYAVLPREVVCTENLTPWK
KLLPCSSKAGLSVLLKADRLFHTSYHSQAVHIRPVCRNARCTSISWELRQTLSVVFDAFITG
QGKKDWSLFRMFSRTLTEPCPLASESRVYVDITTYNQDNETLEVHPPPTTTYQDVILGTRKT
YAIYDLLDTAMINNSRNLNIQLKWKRPPENEAPPVPFLHAQRYVSGYGLQKGELSTLLYNTH
PYRAFPVLLLDTVPWYLRLYVHTLTITSKGKENKPSYIHYQPAQDRLQPHLLEMLIQLPANS
VTKVSIQFERALLKWTEYTPDPNHGFYVSPSVLSALVPSMVAAKPVDWEESPLFNSLFPVSD
GSNYFVRLYTEPLLVNLPTPDFSMPYNVICLTCTVVAVCYGSFYNLLTRTFHIEEPRTGGLA
KRLANLIRRARGVPPL

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FIGURE 240

 ${\tt MGSSSFLVLMVSLVLVTLVAVEGVKEGIEKAGVCPADNVRCFKSDPPQCHTDQDCLGERKCC} \\ {\tt YLHCGFKCVIPVKELEEGGNKDEDVSRPYPEPGWEAKCPGSSSTRCPQK} \\$

FIGURE 241

AAACTCAGCACTTGCCGGAGTGGCTCATTGTTAAGACAAAGGGTGTGCACTTCCTGGCCAGG AAACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCCCAGGACATGCAGAACCTTCC ${\tt TCTAGAACCCGACCCACCACC} \underline{{\tt ATG}} {\tt AGGTCCTGCCTGTGGAGATGCAGGCACCTGAGCCAAGG}$ CTACAGTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCGAGGAGGACAACCATCTA TGCAGAGCCAGCCCAGAGAACAATGCCCTCAACACACAAACCCAGCCCAAGGCCCACACCA ACAGCACAGAGGGCAGCATGGAAGAGGCCCAGAAAAAGAGAAAACCATGGTGAACACACTGTC ACCCAGAGGGCAAGATGCAGGGATGGCCTCTGGCAGGACAGAGGCACAATCATGGAAGAGCC AGGACACAAAGACGACCCAAGGAAATGGGGGCCAGACCAGGAAGCTGACGGCCTCCAGGACG GTGTCAGAGAAGCACCAGGGCAAAGCGGCAACCACAGCCAAGACGCTCATTCCCAAAAGTCA GCACAGAATGCTGGCTCCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGACCA CAGCAGTCATCCCACCTAAGGAGAAGAAACCTCAGGCCACCCCACCCCCTGCCCCTTTCCAG AGCCCCACGACGCAGAGAACCAAAGACTGAAGGCCGCCAACTTCAAATCTGAGCCTCGGTG GGATTTTGAGGAAAAATACAGCTTCGAAATAGGAGGCCTTCAGACGACTTGCCCTGACTCTG TGAAGATCAAAGCCTCCAAGTCGCTGTGGCTCCAGAAACTCTTTCTGCCCAACCTCACTCTC TTCCTGGACTCCAGACACTTCAACCAGAGTGAGTGGGACCGCCTGGAACACTTTGCACCACC ${\tt CTTTGGCTTCATGGAGCTCAACTACTCCTTGGTGCAGAAGGTCGTGACACGCTTCCCTCCAG}$ TGCCCCAGCAGCAGCTGCTCCTGGCCAGCCTCCCGCTGGGAGCCTCCGGTGCATCACCTGT GCCGTGGTGGGCAACGGGGCATCCTGAACAACTCCCACATGGGCCAGGAGATAGACAGTCA $\tt CGACTACGTGTTCCGATTGAGCGGAGCTCTCATTAAAGGCTACGAACAGGATGTGGGGACTC$ GGACATCCTTCTACGGCTTTACCGCCTTCTCCCTGACCCAGTCACTCCTTATATTGGGCAAT CCGGGACTATGAGTGGCTGGAAGCACTGCTTATGAATCAGACGGTGATGTCAAAAAACCTTT TCTGGTTCAGGCACAGACCCCAGGAAGCTTTTCGGGAAGCCCTGCACATGGACAGGTACCTG ${\tt TTGCTGCACCCAGACTTTCTCCGATACATGAAGAACAGGTTTCTGAGGTCTAAGACCCTGGA}$ ${\tt TGGTGCCCACTGGGGGCCCTCCTGCTGCTCACTGCCCTTC}$ CACTACTATGATACATCATGGAAGCGGCTGATCTTTTACATAAACCATGACTTCAAGCTGGA GAGAGAAGTCTGGAAGCGGCTACACGATGAAGGGATAATCCGGCTGTACCAGCGTCCTGGTC CAAGGCACAGGATACAGTGGGAATCTTGAGACTCTTTGGCCATTTCCCATGGCTCAGACTAA GCTCCAAGCCCTTCAGGAGTTCCAAGGGAACACTTGAACCATGGACAAGACTCTCTCAAGAT ${\tt GGCAAATGGCTAATTGAGGTTCTGAAGTTCTTCAGTACATTGCTGTAGGTCCTGAGGCCAGG}$ GATTTTTAATTAAATGGGGTGATGGGTGGCCAATACCACAATTCCTGCTGAAAAACACTCTT CCAGTCCAAAAGCTTCTTGATACAGAAAAAAGAGCCTGGATTTACAGAAACATATAGATCTG GTTTGAATTCCAGATCGAGTTTACAGTTGTGAAATCTTGAAGGTATTACTTAACTTCACTAC AGATTGTCTAGAAGACCTTTCTAGGAGTTATCTGATTCTAGAAGGGTCTATACTTGTCCTTG TCTTTAAGCTATTTGACAACTCTACGTGTTGTAGAAAACTGATAATAATACAAATGATTGTT

FIGURE 242

MRSCLWRCRHLSQGVQWSLLLAVLVFFLFALPSFIKEPQTKPSRHQRTENIKERSLQSLAKP
KSQAPTRARRTTIYAEPAPENNALNTQTQPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAW
KSPEKEKTMVNTLSPRGQDAGMASGRTEAQSWKSQDTKTTQGNGGQTRKLTASRTVSEKHQG
KAATTAKTLIPKSQHRMLAPTGAVSTRTRQKGVTTAVIPPKEKKPQATPPPAPFQSPTTQRN
QRLKAANFKSEPRWDFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLFLPNLTLFLDSRHF
NQSEWDRLEHFAPPFGFMELNYSLVQKVVTRFPPVPQQQLLLASLPAGSLRCITCAVVGNGG
ILNNSHMGQEIDSHDYVFRLSGALIKGYEQDVGTRTSFYGFTAFSLTQSLLILGNRGFKNVP
LGKDVRYLHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEAFREALHMDRYLLLHPDFL
RYMKNRFLRSKTLDGAHWRIYRPTTGALLLLTALQLCDQVSAYGFITEGHERFSDHYYDTSW
KRLIFYINHDFKLEREVWKRLHDEGIIRLYQRPGPGTAKAKN

FIGURE 243

FIGURE 244

 ${\tt MRGPGHPLLLGLLLVLGPSPEQRVEIVPRDLRMKDKFLKHLTGPLYFSPKCSKHFHRLYHNT} \\ {\tt RDCTIPAYYKRCARLLTRLAVSPVCMEDK}$

حدع / حده FIGURE 245

GGGCTGGGCCCGCCGCAGCTCCAGCTGGCCGGCTTGGTCCTGCGGTCCCTTCTCTGGGAGG ${\tt GTGGTACCTGGACCGGAATGGCTCCTGGCATCCGGGGTTTAACTGCGAGTTCTTCACCTTCT}$ GCTGCGGGACCTGCTACCATCGGTACTGCTGCAGGGACCTGACCTTGCTTATCACCGAGAGG CAGCAGAAGCACTGCCTGGCCTTCAGCCCCAAGACCATAGCAGGCATCGCCTCAGCTGTGAT ${\tt CCTCTTTGTTGCTGTTGCCACCACCATCTGCTGCTTCCTGTTCCTGTTGCTACCTGT}$ ACCGCCGGCGCCAGCAGCTCCAGAGCCCATTTGAAGGCCAGGAGATTCCAATGACAGGCATC CCAGTGCAGCCAGTATACCCCATACCCCCAGGACCCCAAAGCTGGCCCTGCACCCCCACAGCC TGGCTTCATGTACCCACCTAGTGGTCCTGCTCCCCAATATCCACTCTACCCAGCTGGGCCCC CAGTCTACAACCCTGCAGCTCCTCCTCCTATATGCCACCACAGCCCTCTTACCCGGGAGCC **TGA**GGAACCAGCCATGTCTCTGCTGCCCCTTCAGTGATGCCAACCTTGGGAGATGCCCTCAT CCTGTACCTGCATCTGGTCCTGGGGGTGGCAGGGTCCTCCAGCCACCAGGCCCCAGACCAA GCCAAGCCCTGGGCCCTACTGGGGACAGAGCCCCCAGGGAAGTGGAACAGGAGCTGAACTAGA ACTATGAGGGGTTGGGGGGGGGCTTGGAATTATGGGCTATTTTTACTGGGGGCAAGGGAGG GAGATGACAGCCTGGGTCACAGTGCCTGTTTTCAAATAGTCCCTCTGCTCCCAAGATCCCAG TCCGTCAGCAGCTGGCCGCTCCTCTCTGGCCTGCCCCACTGGCCACATCTCTGGCCTG CTAGATTAAAGCTGTAAAGACAAA

そり/310 FIGURE 246

MPPAGLRRAAPLTAIALLVLGAPLVLAGEDCLWYLDRNGSWHPGFNCEFFTFCCGTCYHRYC CRDLTLLITERQQKHCLAFSPKTIAGIASAVILFVAVVATTICCFLCSCCYLYRRRQQLQSP FEGQEIPMTGIPVQPVYPYPQDPKAGPAPPQPGFMYPPSGPAPQYPLYPAGPPVYNPAAPPP YMPPQPSYPGA

FIGURE 247

GGGGGAGCTAGGCCGGCGCAGTGGTGGCGGCGCGCAAGGGTGAGGGCGGCCCCAGAA ${\tt CCCCAGGTAGGTAGAGCAAGAAG} \underline{{\tt ATG}} {\tt GTGTTTCTGCCCCTCAAATGGTCCCTTGCAACCATG}$ ${ t TCATTTCTACTTTCCTCACTGTTGGCTCTCTTAACTGTGTCCACTCCTTCATGGTGTCAGAG}$ CACTGAAGCATCTCCAAAACGTAGTGATGGGACACCATTTCCTTGGAATAAAATACGACTTC CTGAGTACGTCATCCCAGTTCATTATGATCTCTTGATCCATGCAAACCTTACCACGCTGACC TTCTGGGGAACCACGAAAGTAGAAATCACAGCCAGTCAGCCCACCAGCACCATCATCCTGCA TAGTCACCACCTGCAGATATCTAGGGCCACCCTCAGGAAGGGAGCTGGAGAGAGGCTATCGG AAGAACCCCTGCAGGTCCTGGAACACCCCCCTCAGGAGCAAATTGCACTGCTGGCTCCCGAG CCCCTCCTTGTCGGGCTCCCGTACACAGTTGTCATTCACTATGCTGGCAATCTTTCGGAGAC CAACACAATTTGAACCCACTGCAGCTAGAATGGCCTTTCCCTGCTTTGATGAACCTGCCTTC AAAGCAAGTTTCTCAATCAAAATTAGAAGAGGCCAAGGCCACCTAGCCATCTCCAATATGCC ATTGGTGAAATCTGTGACTGTTGCTGAAGGACTCATAGAAGACCATTTTGATGTCACTGTGA AGATGAGCACCTATCTGGTGGCCTTCATCATTTCAGATTTTGAGTCTGTCAGCAAGATAACC AAGAGTGGAGTCAAGGTTTCTGTTTATGCTGTGCCAGACAAGATAAATCAAGCAGATTATGC ACTGGATGCTGCGGTGACTCTTCTAGAATTTTATGAGGATTATTTCAGCATACCGTATCCCC TACCCAAACAAGATCTTGCTGCTATTCCCGACTTTCAGTCTGGTGCTATGGAAAACTGGGGA $\tt CTGACAACATATAGAGAATCTGCTCTGTTGTTTGATGCAGAAAAGTCTTCTGCATCAAGTAA$ GCTTGGCATCACAGTGACTGTGGCCCATGAACTGGCCCACCAGTGGTTTGGGAACCTGGTCA CTATGGAATGGTGGAATGATCTTTGGCTAAATGAAGGATTTGCCAAATTTATGGAGTTTGTG TCTGTCAGTGTGACCCATCCTGAACTGAAAGTTGGAGATTATTTCTTTGGCAAATGTTTTGA CGCAATGGAGGTAGATGCTTTAAATTCCTCACACCCTGTGTCTACACCTGTGGAAAATCCTG CTCAGATCCGGGAGATGTTTGATGATGTTTCTTATGATAAGGGAGCTTGTATTCTGAATATG CTAAGGGAGTATCTTAGCGCTGACGCATTTAAAAGTGGTATTGTACAGTATCTCCAGAAGCA TAGCTATAAAAATACAAAAAACGAGGACCTGTGGGATAGTATGGCAAGTATTTGCCCTACAG ATGGTGTAAAAGGGATGGATGGCTTTTGCTCTAGAAGTCAACATTCATCTTCATCCTCACAT ${\tt TGGCATCAGGAAGGGGTGGATGTGAAAACCATGATGAACACTTGGACACTGCAGAGGGGTTT}$ TCCCCTAATAACCATCACAGTGAGGGGGGGGGATGTACACATGAAGCAAGAGCACTACATGA AGGGCTCTGACGGCCCCCGGACACTGGGTACCTGTGGCATGTTCCATTGACATTCATCACC AGCAAATCCAACATGGTCCATCGATTTTTGCTAAAAACAAAACAGATGTGCTCATCCTCCC AGAAGAGGTGGAATGGATCAAATTTAATGTGGGCATGAATGGCTATTACATTGTGCATTACG AATGATCGGGCAAGTCTCATTAACAATGCATTTCAGCTCGTCAGCATTGGGAAGCTGTCCAT TGAAAAGGCCTTGGATTTATCCCTGTACTTGAAACATGAAACTGAAATTATGCCCGTGTTTC GAAACTCAATTCAAGGCCTTCCTCATCAGGCTGCTAAGGGACCTCATTGATAAGCAGACATG GACAGACGAGGGCTCAGTCTCAGAGCAAATGCTGCGGAGTGAACTACTACTCCTCGCCTGTG AATGGAAACTTGAGCCTGCCTGTCGACGTGACCTTGGCAGTGTTTGCTGTGGGGGCCCAGAG CACAGAAGGCTGGGATTTTCTTTATAGTAAATATCAGTTTTCTTTGTCCAGTACTGAGAAAA GCCAAATTGAATTTGCCCTCTGCAGAACCCAAAATAAGGAAAAGCTTCAATGGCTACTAGAT GAAAGCTTTAAGGGAGATAAAATAAAAACTCAGGAGTTTCCACAAATTCTTACACTCATTGG CAGGAACCCAGTAGGATACCCACTGGCCTGGCAATTTCTGAGGAAAAACTGGAACAAACTTG TACAAAAGTTTGAACTTGGCTCATCTTCCATAGCCCACATGGTAATGGGTACAACAAATCAA TTCTCAGCTCCGTTGTGTCCAACAGACAATTGAAACCATTGAAGAAAACATCGGTTGGATGG ${\tt ATAAGAATTTTGATAAAATCAGAGTGTGGCTGCAAAGTGAAAGCTTGAACGTATG}{{\tt TAA}}{\tt AAA}$ TTCCTCCCTTGCCCGGTTCCTGTTATCTCTAATCACCAACATTTTGTTGAGTGTATTTTCAA ACTAGAGATGGCTGTTTTGGCTCCAACTGGAGATACTTTTTTCCCTTCAACTCATTTTTTGA $\tt CTATCCCTGTGAAAAGAATAGCTGTTAGTTTTTCATGAATGGGCTTTTTCATGAATGGGCTA$ TCGCTACCATGTGTTTGTTCATCACAGGTGTTGCCCTGCAACGTAAACCCAAGTGTTGGGT

FIGURE 248

MVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVH YDLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLQVLE HPPQEQIALLAPEPLLVGLPYTVVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTA ARMAFPCFDEPAFKASFSIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVA FIISDFESVSKITKSGVKVSVYAVPDKINQADYALDAAVTLLEFYEDYFSIPYPLPKQDLAA IPDFQSGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELAHQWFGNLVTMEWWNDL WLNEGFAKFMEFVSVSVTHPELKVGDYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFD DVSYDKGACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDG FCSRSQHSSSSSHWHQEGVDVKTMMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPD TGYLWHVPLTFITSKSNMVHRFLLKTKTDVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSL TGLLKGTHTAVSSNDRASLINNAFQLVSIGKLSIEKALDLSLYLKHETEIMPVFQGLNELIP ${\tt MYKLMEKRDMNEVETQFKAFLIRLLRDLIDKQTWTDEGSVSEQMLRSELLLLACVHNYQPCV}$ QRAEGYFRKWKESNGNLSLPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSSTEKSQIEFALC RTQNKEKLQWLLDESFKGDKIKTQEFPQILTLIGRNPVGYPLAWQFLRKNWNKLVQKFELGS SSIAHMVMGTTNQFSTRTRLEEVKGFFSSLKENGSQLRCVQQTIETIEENIGWMDKNFDKIR VWLQSEKLERM

€53/310 FIGURE 249

 ${\tt CAGCCACAGACGGGTC{\color{blue} {\bf ATG}} {\tt AGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCCAC}}$ TGCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCC GACCTACCCCGGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGA CACGTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGCTCTCCAAGGGCTGCACGG AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACCGGATGGGCCCCGGCCTCTCCCTGATC TTGGGCCCCACAGCCCCAGCAGACCCAGGATCCTTGAGGTGCCCAGTCTGCTTGTCTATGG AAGGCTGTCTGGAGGGGACAACAGAAGAGATCTGCCCCAAGGGGACCACACACTGTTATGAT CCAGCCAGGTTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCGTGGGTATGACTGAGA ACTGCAATAGGAAAGATTTTCTGACCTGTCATCGGGGGACCACCATTATGACACACGGAAAC TTGGCTCAAGAACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGGCAGGT GTGTCAGGAGACGCTGCTGCTCATAGATGTAGGACTCACATCAACCCTGGTGGGGACAAAAG GCTGCAGCACTGTTGGGGCTCAAAATTCCCAGAAGACCACCATCCACTCAGCCCCTCCTGGG GTGCTTGTGGCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG CAGCGTTCTGCTGAACTCCCTCCTCCAAGCTGCCCCTGTCCCAGGAGACCGGCAGTGTC ${\tt CTACCTGTGCAGCCCCTTGGAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCCCAGG}$ GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAAT GAGCATTCAGGGCTGCGTGGCCCAACCTTCCAGCTTCTTGTTGAACCACACCAGACAAATCG GGGGCTGAGGGCCTGGAGTCTCTCACTTGGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTG $\tt GTGGGGAGTGGTTTGCCCTTCCTGC{\color{red}{TAA}}CTCTATTACCCCCACGATTCTTCACCGCTGCTGA$ CCACCCACACTCAACCTCCTCTGACCTCATAACCTAATGGCCTTGGACACCAGATTCTTTC ACACTGGGGAGAGCCTGGAGCATCCGGACTTGCCCTATGGGAGAGGGGACGCTGGAGGAGTG GCTGCATGTATCTGATAATACAGACCCTGTCCTTTCA

FIGURE 250

MSAVLLLALLGFILPLPGVQALLCQFGTVQHVWKVSDLPRQWTPKNTSCDSGLGCQDTLMLI ESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDFCNNLVNSLPLWAPQP PADPGSLRCPVCLSMEGCLEGTTEEICPKGTTHCYDGLLRLRGGGIFSNLRVQGCMPQPGCN LLNGTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSNTEMCEVGQVCQETL LLIDVGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCNSASSSSVLLN SLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLSGGGLSTKMSIQGC VAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESLTWGVGLALAPALWWGVVCPSC

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FIGURE 251

CAGGATGAGGGGGAATCTGGCCCTGGTGGGCGTTCTAATCAGCCTGGCCTTCCTGTCACTGCTG CCATCTGGACATCCTCAGCCGGCTGCGGATGACGCCTGCTCTGTGCAGATCCTCGTCCCTGG CCTCAAAGGGGATGCGGGAGAGAGGGAGACAAAGGCGCCCCCGGACGGCCTGGAAGAGTCG GCCCCACGGGAGAAAAGGAGACATGGGGGACAAAGGACAGAAAGGCAGTGTGGGTCGTCAT GGAAAAATTGGTCCCATTGGCTCTAAAGGTGAGAAAGGAGATTCCGGTGACATAGGACCCCC AGATGGACAACCAGGTCTCTCAGCTGACCAGCGAGCTCAAGTTCATCAAGAATGCTGTCGCC GGTGTGCGCGAGACGGAGAGCAAGATCTACCTGCTGGTGAAGGAGGAGAAGCGCTACGCGGA CGCCAGCTGTCCTGCCAGGGCCGCGGGGGCACGCTGAGCATGCCCAAGGACGAGGCTGCCA ATGGCCTGATGGCCGCATACCTGGCGCAAGCCGGCCTGGCCCGTGTCTTCATCGGCATCAAC GACCTGGAGAAGGAGGGCGCCTTCGTGTACTCTGACCACTCCCCCATGCGGACCTTCAACAA GTGGCGCAGCGTGAGCCCAACAATGCCTACGACGAGGAGGACTGCGTGGAGATGGTGGCCT CGGGCGGCTGGAACGACGTGGCCTGCCACACCACCATGTACTTCATGTGTGAGTTTGACAAG GAGAACATGTGAGCCTCAGGCTGGGGCTGCCCATTGGGGGCCCCACATGTCCCTGCAGGGTT GGCAGGGACAGACCCAGGCCAGCCAGGGAGCTGTCCCTCTGTGAAGGGTGGAG GCTCACTGAGTAGAGGGCTGTTGTCTAAACTGAGAAAATGGCCTATGCTTAAGAGGAAAATG AAAGTGTTCCTGGGGTGCTGTCTCTGAAGAAGCAGAGTTTCATTACCTGTATTGTAGCCCCA ATGTCATTATGTAATTATTACCCAGAATTGCTCTTCCATAAAGCTTGTGCCTTTGTCCAAGC

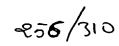


FIGURE 252

MRGNLALVGVLISLAFLSLLPSGHPQPAGDDACSVQILVPGLKGDAGEKGDKGAPGRPGRVG
PTGEKGDMGDKGQKGSVGRHGKIGPIGSKGEKGDSGDIGPPGPNGEPGLPCECSQLRKAIGE
MDNQVSQLTSELKFIKNAVAGVRETESKIYLLVKEEKRYADAQLSCQGRGGTLSMPKDEAAN
GLMAAYLAQAGLARVFIGINDLEKEGAFVYSDHSPMRTFNKWRSGEPNNAYDEEDCVEMVAS
GGWNDVACHTTMYFMCEFDKENM

FIGURE 253

AGTGACTGCAGCCTTCCTAGATCCCCTCCACTCGGTTTCTCTCTTTGCAGGAGCACCGGCAG CACCAGTGTGTGAGGGGAGCAGCGGTCCTAGCCAGTTCCTTGATCCTGCCAGACCACC ${\tt CAGCCCCGGCACAGAGCTGCTCCACAGGCACC} \underline{{\tt ATG}} {\tt AGGATCATGCTGCTATTCACAGCCAT}$ ${\tt TTCCTGGCGGGGCCGCAGCAGAGGGGATCCAGATCTCTACCAGCTGCTCCAGAGACTCTTC}$ AAAAGCCACTCATCTCTGGAGGGATTGCTCAAAGCCCTGAGCCAGGCTAGCACAGATCCTAA GGAATCAACATCTCCCGAGAAACGTGACATGCATGACTTCTTTGTGGGACTTATGGGCAAGA ${\tt GGAGCGTCCAGCCAGAGGGAAAGACAGGACCTTTCTTACCTTCAGTGAGGGTTCCTCGGCCC}$ $\tt CTTCATCCCAATCAGCTTGGATCCACAGGAAAGTCTTCCCTGGGAACAGAGGAGCAGAGACCC$ ${\tt TTTA} \underline{{\tt TAA}} {\tt GACTCTCCTACGGATGTGAATCAAGAGAACGTCCCCAGCTTTGGCATCCTCAAGT}$ ATCCCCCGAGAGCAGAATAGGTACTCCACTTCCGGACTCCTGGACTGCATTAGGAAGACCTC $\tt TTTCCCTGTCCCAATCCCCAGGTGCGCACGCTCCTGTTACCCTTTTCTCTTCTCTTGT$ AACATTCTTGTGCTTTGACTCCTTCTCCATCTTTTCTACCTGACCCTGGTGTGGAAACTGCA TAGTGAATATCCCCAACCCCAATGGGCATTGACTGTAGAATACCCTAGAGTTCCTGTAGTGT CCTACATTAAAAATATAATGTCTCTCTATTCCTCAACAATAAAGGATTTTTGCATATGAA

FIGURE 254

MRIMLLFTAILAFSLAQSFGAVCKEPQEEVVPGGGRSKRDPDLYQLLQRLFKSHSSLEGLLK ALSQASTDPKESTSPEKRDMHDFFVGLMGKRSVQPEGKTGPFLPSVRVPRPLHPNQLGSTGK SSLGTEEQRPL

५५७ / ३१० FIGURE 255

GGGCGTCTCCGGCTGCTCCTATTGAGCTGTCTGCTCGCTGTGCCCGCTGTGCCTGCTGTGCC CGCGCTGTCGCCGCTACCGCGTCTGCTGGACGCGGGAGACGCCAGCGAGCTGGTGATTG GAGCCCTGCGGAGAGCTCAAGCGCCCAGCTCTGCCCCAGGAGCCCAGGCTGCCCCGTGAGTC CCATAGTTGCTGCAGGAGTGGAGCCATGAGCTGCGTCCTGGGTGTGTCATCCCCTTGGGGC TGCTGTTCCTGGTCTGCGGATCCCAAGGCTACCTCCTGCCCAACGTCACTCTCTTAGAGGAG CTGCTCAGCAAATACCAGCACAACGAGTCTCACTCCCGGGTCCGCAGAGCCATCCCCAGGGA GGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTTCGGGGCCAGGTGCAGCCTCAGGCCT CCAACATGGAGTACATGGTGAGCGCCGGCTCCGGCCGCAGAGGCTGGCACCGGGGGTGGGGC TTGAGACAGGGTCTCACTCTGCCACTGACGCTGGAGTGCAATGGCACAATCGTCATGCCCTG AAACCT<u>TAG</u>ACTCCCGGGGTTAAGCGATCCTGCTTCAGCCTCCCAAGTAGCTGGAACTACAG GCATGCACCATGGTGCCCAGCTAGATTTTAAATATTTTTGTGGAGATGGGGGTCTTGCTACGT TGCCCAGGCTGGTCTTGAACTCCTAGGCTCAAGCAATCCTCCTGCCTCAGCCTCTCAAAGTG CTAGGATTATAGGCATGAGTCACCCTGTCTGGCTCTGGCTCTGTTCTTAACATTCTGCCAAA ACAACACGTGGGTTCCCTGTGCAGAGCCTGCCTCGTTGCCTTCATGTCACTCTTGGTAGC TCCACTGGGAACACAGCTCTCAGCCTTTCCCACCTGGAGGCAGAGTGGGGAGGGGCCCAGGG CTGGGCTTTGCTGATGCTGATCTCAGCTGTGCCACACGCTAGCTGCACCACCCTGACTTCTC GTGAGATAAGTCGAGGCTGTGAAGGGCCCGGCACAGACTGACCTGCCTCCCCAACCCCTAGG CTTTGCTAACCGGGAAAGGAGCTAACGGTGACAGAAGACAGCCAAGGTCAACCCTCCCGGGT GATTGTGATGGGTGTTCCAGGTGTGGTTGGGCGATGCTGCTACTTGACCCCAAGCTCCAGTG TGGAAACTTCCTTCCTGGCTGGTTTTCCAGAACTACAGAGGAATGGACCACAGTCTTCCAGG GTCCCTCCTCGTCCACCAACCGGGAGCCTCCACCTTGGCCATCCGTCAGCTATGAATGGCTT TTTAAACAAACCCACGTCCCAGCCTGGGTAACATGGTAAAGCCCCGTCTCTACAAAAAAATC CAAGTTAGCCGGGCATGGTGCGCACCTGTAGTCCCAGCTGCAGTGGGACTGAGGTGGAG GTGGAGGTGGGGGGGGGGCTGAGGAAGGAGGATCGCTTGAGCCTGGGAAGTCGAGGCTGC AGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCAAAAA

FIGURE 256

MSCVLGGVIPLGLLFLVCGSQGYLLPNVTLLEELLSKYQHNESHSRVRRAIPREDKEEILML HNKLRGQVQPQASNMEYMVSAGSGRRGWHRGWGLGHQPALFPSQLCSPASACDGWLRVSSGR GGSRLCSVLFVCFETGSHSATDAGVQWHNRHALKP

FIGURE 257

 ${\tt MGSGLPLVLLLTLLGSSHGTGPGMTLQLKLKESFLTNSSYESSFLELLEKLCLLLHLPSGTS} \\ {\tt VTLHHARSQHHVVCNT}$

264/310 FIGURE 260

 $\verb|MIGYYLILFLMWGSSTVFCVLLIFTIAEASFSVENECLVDLCLLRICYKLSGVPNQCRVPLP| \\ SDCSK$

~ 65/310 FIGURE 261

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGGAGCACCACCGGAGCCCTTGAGACATCCTT ${\tt GAGAAGAGCCACAGCATAAGAGACTGCCCTGCTTGGTGTTTTGCAGG} \underline{{\tt ATG}} {\tt ATGGTGGCCCTT}$ CGAGGAGCTTCTGCATTGCTGGTTCTGTTCCTTGCAGCTTTTCTGCCCCCGCCGCAGTGTAC CCAGGACCCAGCCATGGTGCATTACATCTACCAGCGCTTTCGAGTCTTGGAGCAAGGGCTGG AAAAATGTACCCAAGCAACGAGGGCATACATTCAAGAATTCCAAGAGTTCTCAAAAAATATA ${\tt TCTGTCATGCTGGGAAGATGTCAGACCTACACAAGTGAGTACAAGAGTGCAGTGGGTAACTT}$ ACGAGTGCATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCCAAGAAGCTGAAGAA GAGAAAAAGATCCGGACTCTGCTGAATGCAAGCTGTGACAACATGCTGATGGGCATAAAGTC TTTGAAAATAGTGAAGAAGATGATGGACACACATGGCTCTTGGATGAAAGATGCTGTCTATA ACTCTCCAAAGGTGTACTTATTAATTGGATCCAGAAACAACACTGTTTGGGAATTTGCAAAC ATACGGGCATTCATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCCTAACACTTTC CTGGCAGGGAACAGGCCAAGTGATCTACAAAGGTTTTCTATTTTTCATAACCAAGCAACTT CTAATGAGATAATCAAATATAACCTGCAGAAGAGGGACTGTGGAAGATCGAATGCTGCTCCCA GGAGGGGTAGGCCGAGCATTGGTTTACCAGCACTCCCCCTCAACTTACATTGACCTGGCTGT ${\tt GGATGAGCATGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTTGGTTCTCA}$ CAAAGATTGAGCCGGGCACACTGGGAGTGGAGCATTCATGGGATACCCCATGCAGAAGCCAG GATGCTGAAGCCTCATTCCTCTTGTGTGGGGTTCTCTATGTGGTCTACAGTACTGGGGGCCA GGGCCCTCATCGCATCACCTGCATCTATGATCCACTGGGCACTATCAGTGAGGAGGACTTGC CCAACTTGTTCTTCCCCAAGAGACCAAGAAGTCACTCCATGATCCATTACAACCCCAGAGAT AAGCAGCTCTATGCCTGGAATGAAGGAAACCAGATCATTTACAAACTCCAGACAAAGAGAAA ${\tt GCTGCCTCTGAAG}$ ${\tt TAA}$ ${\tt TGCATTACAGCTGTGAGAAAGAGCACTGTGGCTTTGGCAGCTGTTC}$ ${\tt AGTGTGTAGAAGTGGAAATACGTATGCCTCCTTTCCCAAATGTCACTGCCTTAGGTATCTTC}$ CAAGAGCTTAGATGAGAGCATATCATCAGGAAAGTTTCAACAATGTCCATTACTCCCCCAAA ${\tt CCTCCTGGCTCTCAAGGATGACCACATTCTGATACAGCCTACTTCAAGCCTTTTGTTTTACT}$ $\tt CCCTAATATTCACCACTGGCTTTTCTCTCCCCTGGCCTTTGCTGAAGCTCTTCCCTCTTTTT$ CAAATGTCTATTGATATTCTCCCATTTTCACTGCCCAACTAAAATACTATTAATATTTCTTT CTTTTCTTTTCTTTTTTGAGACAAGGTCTCACTATGTTGCCCAGGCTGGTCTCAAACTCC AGAGCTCAAGAGATCCTCCTGCCTCAGCCTCCTAAGTACCTGGGATTACAGGCATGTGCCAC CACACCTGGCTTAAAATACTATTTCTTATTGAGGTTTAACCTCTATTTCCCCTAGCCCTGTC CTTCCACTAAGCTTGGTAGATGTAATAATAAAGTGAAAATATTAACATTTGAATATCGCTTT ${\tt CCAGGTGTGGAGTGTTTGCACATCATTGAATTCTCGTTTCACCTTTGTGAAACATGCACAAG}$ TCTTTACAGCTGTCATTCTAGAGTTTAGGTGAGTAACACAATTACAAAGTGAAAGATACAGC TAGAAAATACTACAAATCCCATAGTTTTTCCATTGCCCAAGGAAGCATCAAATACGTATGTT ${\tt TGTTCACCTACTCTTATAGTCAATGCGTTCATCGTTTCAGCCTAAAAATAATAGTCTGTCCC}$ TTTAGCCAGTTTTCATGTCTGCACAAGACCTTTCAATAGGCCTTTCAAATGATAATTCCTCC ${\tt AGAAAACCAGTCTAAGGGTGAGGACCCCAACTCTAGCCTCTTGTCTTGTCTTGTCTTGT}$

€66/210 FIGURE 262

MMVALRGASALLVLFLAAFLPPPQCTQDPAMVHYIYQRFRVLEQGLEKCTQATRAYIQEFQE FSKNISVMLGRCQTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECIVSEDKTLAEMLL QEAEEEKKIRTLLNASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNSPKVYLLIGSRNNTV WEFANIRAFMEDNTKPAPRKQILTLSWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVED RMLLPGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKIEPGTLGVEHSWDT PCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIH YNPRDKQLYAWNEGNQIIYKLQTKRKLPLK

e 67/310

FIGURE 263

 $\tt GGGCGCCGCGTACTCACTAGCTGAGGTGGCAGTGGTTCCACCAAC {\color{red} {\bf ATG}} GAGCTCTCGCAGA$ TGTCGGAGCTCATGGGGCTGTCGGTGTTGCTTGGGCTGCTGGCCCTGATGGCGACGGCGGCG AAATGGATTTCCACCTGACAAATCTTCGGGATCCAAGAAGCAGAACAATATCAGCGGATTC GGAAGGAGAAGCCTCAACAACACAACTTCACCCACCGCCTCCTGGCTGCAGCTCTGAAGAGC CACAGCGGGAACATATCTTGCATGGACTTTAGCAGCAATGGCAAATACCTGGCTACCTGTGC AGATGATCGCACCATCCGCATCTGGAGCACCAAGGACTTCCTGCAGCGAGAGCACCGCAGCA TGAGAGCCAACGTGGAGCTGGACCACGCCACCCTGGTGCGCTTCAGCCCTGACTGCAGAGCC TTCATCGTCTGGCTGGCCAACGGGGACACCCTCCGTGTCTTCAAGATGACCAAGCGGGAGGA TGGGGGCTACACCTTCACAGCCACCCCAGAGGACTTCCCTAAAAAGCACAAGGCGCCTGTCA ${\tt TCGACATTGGCATTGCTAACACAGGGAAGTTTATCATGACTGCCTCCAGTGACACCACTGTC}$ ACACGCTGCTGTATCTCCCTGTGGCAGATTTGTAGCCTCGTGTGGCTTCACCCCAGATGTGA AGGTTTGGGAAGTCTGCTTTGGAAAGAAGGGGGGGTTCCAGGAGGTGGTGCGAGCCTTCGAA $\tt CTAAAGGGCCACTCCGCGGGTGTGCACTCGTTTGCTTTCTCCAACGACTCACGGAGGATGGC$ TTCTGTCTCCAAGGATGGTACATGGAAACTGTGGGACACAGATGTGGAATACAAGAAGAAGC AGGACCCCTACTTGCTGAAGACAGGCCGCTTTGAAGAGGCGGCGGGGTGCCGCCGTGCCGC CTGGCCCTCTCCCCCAACGCCCAGGTCTTGGCCTTGGCCAGTGGCAGTAGTATTCATCTCTA ${\tt CAATACCCGGCGGGGGGAGAAGGAGGAGTGCTTTGAGCGGGTCCATGGCGAGTGTATCGCCA}$ ACTTGTCCTTTGACATCACTGGCCGCTTTCTGGCCTCCTGTGGGGACCGGGCGGTGCGGCTG CTCCAACGAGAGCACCCGCCAGAGGCTGCAGCAGCTGACCCAGGCCCAAGAGACCCTGA ${\tt AGAGCCTGGGTGCCCTGAAGAAG}$ ${\tt CTCTGGGAGGGCCCGGCGCAGAGGATTGAGGAGGAG}$ GGATCTGGCCTCCTCATGGCACTGCTGCCATCTTTCCTCCCAGGTGGAAGCCTTTCAGAAGG AGTCTCCTGGTTTTCTTACTGGTGGCCCTGCTTCTTCCCATTGAAACTACTCTTGTCTACTT AGGTCTCTCTTCTTGCTGGCTGTGACTCCTCCCTGACTAGTGGCCAAGGTGCTTTTCTTC CTCCCAGGCCCAGTGGGTGGAATCTGTCCCCACCTGGCACTGAGGAGAATGGTAGAGAGGAG AGGAGAGAGAGAGATGTGATTTTTGGCCTTGTGGCAGCACATCCTCACACCCAAAGAAG TTTGTAAATGTTCCAGAACAACCTAGAGAACACCTGAGTACTAAGCAGCAGTTTTGCAAGGA ${\tt TGGGAGACTGGGATAGCTTCCCATCACAGAACTGTGTTCCATCAAAAAGACACTAAGGGATT}$ ${\tt TCCTTCTGGGCCTCAGTTCTATTTGTAAGATGGAGAATAATCCTCTCTGTGAACTCCTTGCA}$ AAGATGATATGAGGCTAAGAGAATATCAAGTCCCCAGGTCTGGAAGAAAAGTAGAAAAGAGT AGTACTATTGTCCAATGTCATGAAAGTGGTAAAAGTGGGAACCAGTGTGCTTTGAAACCAAA TTAGAAACACATTCCTTGGGAAGGCAAAGTTTTCTGGGACTTGATCATACATTTTATATGGT TGGGACTTCTCTCTCGGGAGATGATATCTTGTTTAAGGAGACCTCTTTTCAGTTCATCAAG

€ 68 /310 FIGURE 264

MELSQMSELMGLSVLLGLLALMATAAVARGWLRAGEERSGRPACQKANGFPPDKSSGSKKQK
QYQRIRKEKPQQHNFTHRLLAAALKSHSGNISCMDFSSNGKYLATCADDRTIRIWSTKDFLQ
REHRSMRANVELDHATLVRFSPDCRAFIVWLANGDTLRVFKMTKREDGGYTFTATPEDFPKK
HKAPVIDIGIANTGKFIMTASSDTTVLIWSLKGQVLSTINTNQMNNTHAAVSPCGRFVASCG
FTPDVKVWEVCFGKKGEFQEVVRAFELKGHSAAVHSFAFSNDSRRMASVSKDGTWKLWDTDV
EYKKKQDPYLLKTGRFEEAAGAAPCRLALSPNAQVLALASGSSIHLYNTRRGEKEECFERVH
GECIANLSFDITGRFLASCGDRAVRLFHNTPGHRAMVEEMQGHLKRASNESTRQRLQQQLTQ
AQETLKSLGALKK

e69/310

FIGURE 265

 ${\tt CAGTGTTTTGCCTTCACCCCAAGTGACC} \underline{{\tt ATG}} {\tt AGAGGTGCCACGCGAGTCTCAATCATGCTCC}$ ${\tt TCCTAGTAACTGTGTCTGACTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGT}$ GGGGCAGCCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCT GGGGCGGGAAGGCGAGCCACCCCGGCAGCCACAAGGTCCCCTTCTTCAGGAAACGCA AGCACCACACCTGTCCTTGCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTAC ${\tt CGCTGCTCCATGGACTTGAAGAACATCAATTTT}$ CCATCCTTTTCCTGAGCACAGCCTGGATTTTTATTTCTGCCATGAAACCCAGCTCCCATGAC TCTCCCAGTCCCTACACTGACTACCCTGATCTCTTGTCTAGTACGCACATATGCACACAG GCAGACATACCTCCCATCATGACATGGTCCCCAGGCTGGCCTGAGGATGTCACAGCTTGAGG CTGTGGTGTGAAAGGTGGCCAGCCTGGTTCTCTCTCCCTGCTCAGGCTGCCAGAGAGGTGGTA AATGGCAGAAAGGACATTCCCCCTCCCCTCCCCAGGTGACCTGCTCTCTTTCCTGGGCCCTG $\tt CCCCTCTCCCCACATGTATCCCTCGGTCTGAATTAGACATTCCTGGGCACAGGCTCTTGGGT$ GCATTGCTCAGAGTCCCAGGTCCTGGCCTGACCCTCAGGCCCTTCACGTGAGGTCTGTGAGG ${\tt ACCAATTTGTGGGTAGTTCATCTTCCCTCGATTGGTTAACTCCTTAGTTTCAGACCACAGAC}$ ${\tt TCAAGATTGGCTCTTCCCAGAGGCAGCAGCAGTCACCCCAAGGCAGGTGTAGGGAGCCCA}$ ${\tt GGGAGGCCAATCAGCCCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCCTGTGA}$ ${\tt CCTGTGACCTTCTGCCAGAATTGTCATGCCTCTGAGGCCCCCTCTTACCACACTTTACCAGT}$ TAACCACTGAAGCCCCCAATTCCCACAGCTTTTCCATTAAAATGCAAATGGTGGTGGTTCAA TCTAATCTGATATTGACATATTAGAAGGCAATTAGGGTGTTTCCTTAAACAACTCCTTTCCA ${\tt AGGATCAGCCCTGAGAGCAGGTTGGTGACTTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGG}$ TGGGAGCAAGGGACAGGGCAGGGGCTGAAAGGGGCACTGATTCAGACCAGGGAGG CAACTACACCAACATGCTGGCTTTAGAATAAAAGCACCAACTGAAAAAA

 ${\tt MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEECHP} \\ {\tt GSHKVPFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF}$

ペキイ/310 FIGURE 267

TGCTGCCTTGGCATTGCTGCCAACACAGACGTGTTTCTGTCCAAGCCCCAGAAAGCGG CCCTGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTTCAAA GCAAAGGAGCTATGGGAAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTTT CCTCTGTCGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGGCG TCCCCCTCTATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTTCCAGCCTTAT TTCAAAGGAGAAATCTTCCTGGATGAAAAGAAAAGTTCTATGGTCCACAAAGGCGGAAGAT ${\tt GCTTCTCTGGAAACCTGGAAGGAGAAGGCTTCATCCTTGGGGGAGTTTTCGTGGTGGGATCA}$ GGAAAGCAGGGCATTCTTCTTGAGCACCGAGAAAAAGAATTTGGAGACAAAGTAAACCTACT ${\tt TTCTGTTCTGGAAGCTGCTAAGATGATCAAACCACAGACTTTGGCCTCAGAGAAAAAA} {\tt \underline{TGA}} {\tt TGA} {\tt$ TGTGTGAAACTGCCCAGCTCAGGGATAACCAGGGACATTCACCTGTGTTCATGGGATGTATT GTTTCCACTCGTGTCCCTAAGGAGTGAGAAACCCATTTATACTCTACTCTCAGTATGGATTA TTAATGTATTTTAATATTCTGTTTAGGCCCACTAAGGCAAAATAGCCCCAAAACAAGACTGA CAAAAATCTGAAAAACTAATGAGGATTATTAAGCTAAAACCTGGGAAATAGGAGGCTTAAAA ${\tt TTGACTGCCAGGCTGGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGG}$ TGAGCAAGTCACTTGAGGTCGGGAGTTCGAGACCAGCCTGAGCAACATGGCGAAACCCCGTC TCTACTAAAAATACAAAAATCACCCGGGTGTGGTGGCAGCCACCTGTAGTCCCAGCTACCCG GGAGGCTGAGGCAGGAGATCACTTGAACCTGGGAGGTTGCGGTGAGCTGAGATCA

MSFLQDPSFFTMGMWSIGAGALGAAALALLLANTDVFLSKPQKAALEYLEDIDLKTLEKEPR TFKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDF QPYFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGVWYNFFRAWNGGFSGNLEGEGFILGGVFV VGSGKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK e73/310

FIGURE 269

e74/510

FIGURE 270

MANPGLGLLLALGLPFLLARWGRAWGQIQTTSANENSTVLPSSTSSSSDGNLRPEAITAIIV VFSLLAALLLAVGLALLVRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

حَّرُح \رُحَارِ \ FIGURE 271

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FIGURE 272

 ${\tt MTFFLSLLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGK}\\ {\tt GIVKGRNLDSRGLILGAEAWGRGVKKNT}$

FIGURE 273

 ${\tt GCCAGGAATAACTAGAGGGAACA} \underline{{\tt ATG}} {\tt GGGTTATTCAGAGGTTTTGTTTTCCTCTTAGTTCT}$ GTGCCTGCTGCACCAGTCAAATACTTCCTTCATTAAGCTGAATAATAATGGCTTTGAAGATA TTGTCATTGTTATAGATCCTAGTGTGCCAGAAGATGAAAAAAATAATTGAACAAATAGAGGAT ATGGTGACTACAGCTTCTACGTACCTGTTTGAAGCCACAGAAAAAGATTTTTTTCAAAAA TGTATCTATATTAATTCCTGAGAATTGGAAGGAAAATCCTCAGTACAAAAGGCCAAAACATG AAAACCATAAACATGCTGATGTTATAGTTGCACCACCTACACTCCCAGGTAGAGATGAACCA TACACCAAGCAGTTCACAGAATGTGGAGAGAAAGGCGAATACATTCACTTCACCCCTGACCT TCTACTTGGAAAAAAAAAATGAATATGGACCACCAGGCAAACTGTTTGTCCATGAGTGGG CTCACCTCCGGTGGGGAGTGTTTGATGAGTACAATGAAGATCAGCCTTTCTACCGTGCTAAG TCAAAAAAATCGAAGCAACAAGGTGTTCCGCAGGTATCTCTGGTAGAAATAGAGTTTATAA GTGTCAAGGAGCAGCTGTCTTAGTAGAGCATGCAGAATTGATTCTACAACAAAACTGTATG GAAAAGATTGTCAATTCTTTCCTGATAAAGTACAAACAGAAAAAGCATCCATAATGTTTATG CAAAGTATTGATTCTGTTGAATTTTGTAACGAAAAAACCCATAATCAAGAAGCTCCAAG CCTACAAAACATAAAGTGCAATTTTAGAAGTACATGGGAGGTGATTAGCAATTCTGAGGATT TTAAAAACACCATACCCATGGTGACACCACCTCCTCCACCTGTCTTCTCATTGCTGAAGATC AGTCAAAGAATTGTGTGCTTAGTTCTTGATAAGTCTGGAAGCATGGGGGGTAAGGACCGCCT AAATCGAATGAATCAAGCAGCAAAACATTTCCTGCTGCAGACTGTTGAAAATGGATCCTGGG TGGGGATGGTTCACTTTGATAGTACTGCCACTATTGTAAATAAGCTAATCCAAATAAAAAGC AGTGATGAAAGAAACACACTCATGGCAGGATTACCTACATATCCTCTGGGAGGAACTTCCAT CTGCTCTGGAATTAAATATGCATTTCAGGTGATTGGAGAGCTACATTCCCAACTCGATGGAT CCGAAGTACTGCTGACTGATGGGGAGGATAACACTGCAAGTTCTTGTATTGATGAAGTG AAACAAAGTGGGGCCATTGTTCATTTATTGCTTTGGGAAGAGCTGCTGATGAAGCAGTAAT AGAGATGAGCAAGATAACAGGAGGAAGTCATTTTTATGTTTCAGATGAAGCTCAGAACAATG GCCTCATTGATGCTTTTGGGGCTCTTACATCAGGAAATACTGATCTCTCCCAGAAGTCCCTT CAGCTCGAAAGTAAGGGATTAACACTGAATAGTAATGCCTGGATGAACGACACTGTCATAAT TGATAGTACAGTGGGAAAGGACACGTTCTTTCTCATCACATGGAACAGTCTGCCTCCCAGTA TTTCTCTCTGGGATCCCAGTGGAACAATAATGGAAAATTTCACAGTGGATGCAACTTCCAAA ATGGCCTATCTCAGTATTCCAGGAACTGCAAAGGTGGGCACTTGGGCATACAATCTTCAAGC CAAAGCGAACCCAGAAACATTAACTATTACAGTAACTTCTCGAGCAGCAAATTCTTCTGTGC CTCCAATCACAGTGAATGCTAAAATGAATAAGGACGTAAACAGTTTCCCCAGCCCAATGATT GTTTACGCAGAAATTCTACAAGGATATGTACCTGTTCTTGGAGCCAATGTGACTGCTTTCAT TGAATCACAGAATGGACATACAGAAGTTTTGGAACTTTTGGATAATGGTGCAGGCGCTGATT CTTTCAAGAATGATGGAGTCTACTCCAGGTATTTTACAGCATATACAGAAAATGGCAGATAT AGCTTAAAAGTTCGGGCTCATGGAGGAGCAAACACTGCCAGGCTAAAATTACGGCCTCCACT GAATAGAGCCGCGTACATACCAGGCTGGGTAGTGAACGGGGAAATTGAAGCAAACCCGCCAA GACCTGAAATTGATGAGGATACTCAGACCACCTTGGAGGATTTCAGCCGAACAGCATCCGGA GGTGCATTTGTGGTATCACAAGTCCCAAGCCTTCCCTTGCCTGACCAATACCCACCAAGTCA AATCACAGACCTTGATGCCACAGTTCATGAGGATAAGATTATTCTTACATGGACAGCACCAG GAGATAATTTTGATGTTGGAAAAGTTCAACGTTATATCATAAGAATAAGTGCAAGTATTCTT GATCTAAGAGACAGTTTTGATGATGCTCTTCAAGTAAATACTACTGATCTGTCACCAAAGGA GGCCAACTCCAAGGAAAGCTTTGCATTTAAACCAGAAAATATCTCAGAAGAAAATGCAACCC ACATATTTATTGCCATTAAAAGTATAGATAAAAGCAATTTGACATCAAAAGTATCCAACATT GCACAAGTAACTTTGTTTATCCCTCAAGCAAATCCTGATGACATTGATCCTACACCTACTCC TACTCCTACTCCTGATAAAAGTCATAATTCTGGAGTTAATATTTCTACGCTGGTAT TGTCTGTGATTGGGTCTGTTAATTGTTAACTTTATTTTAAGTACCACCATT \underline{TGA} ACCTTA AAAGGATATTTCTGAATCTTAAAATTCATCCCATGTGTGATCATAAACTCATAAAAATAATT TTAAGATGTCGGAAAAGGATACTTTGATTAAATAAAAACACTCATGGATATGTAAAAACTGT CAAGATTAAAATTTAATAGTTTCATTTATTTGTTATTTTGTAAGAAATAGTGATGAAC AAAGATCCTTTTTCATACTGATACCTGGTTGTATATTATTTGATGCAACAGTTTTCTGAAAT

そ年8/310 FIGURE 274

MGLFRGFVFLLVLCLLHQSNTSFIKLNNNGFEDIVIVIDPSVPEDEKIIEQIEDMVTTASTY
LFEATEKRFFFKNVSILIPENWKENPQYKRPKHENHKHADVIVAPPTLPGRDEPYTKQFTEC
GEKGEYIHFTPDLLLGKKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATR
CSAGISGRNRVYKCQGGSCLSRACRIDSTTKLYGKDCQFFPDKVQTEKASIMFMQSIDSVVE
FCNEKTHNQEAPSLQNIKCNFRSTWEVISNSEDFKNTIPMVTPPPPPVFSLLKISQRIVCLV
LDKSGSMGGKDRLNRMNQAAKHFLLQTVENGSWVGMVHFDSTATIVNKLIQIKSSDERNTLM
AGLPTYPLGGTSICSGIKYAFQVIGELHSQLDGSEVLLLTDGEDNTASSCIDEVKQSGAIVH
FIALGRAADEAVIEMSKITGGSHFYVSDEAQNNGLIDAFGALTSGNTDLSQKSLQLESKGLT
LNSNAWMNDTVIIDSTVGKDTFFLITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPG
TAKVGTWAYNLQAKANPETLTITVTSRAANSSVPPITVNAKMNKDVNSFPSPMIVYAEILQG
YVPVLGANVTAFIESQNGHTEVLELLDNGAGADSFKNDGVYSRYFTAYTENGRYSLKVRAHG
GANTARLKLRPPLNRAAYIPGWVVNGEIEANPPRPEIDEDTQTTLEDFSRTASGGAFVVSQV
PSLPLPDQYPPSQITDLDATVHEDKIILTWTAPGDNFDVGKVQRYIIRISASILDLRDSFDD
ALQVNTTDLSPKEANSKESFAFKPENISEENATHIFIAIKSIDKSNLTSKVSNIAQVTLFIP

セキら/30 FIGURE 275

 $\tt CTCCTTAGGTGGAAACCCTGGGAGTAGAGTACTGACAGCAAAGACCGGGAAAGACCATACGTCCCCGG$ GCAGGGGTGACAACAGGTGTCATCTTTTTGATCTCGTGTGTGGCTGCCTTCCTATTTCAAGGAAAGAC GCCAAGGTAATTTTGACCCAGAGGAGCAATGATGTAGCCACCTCCTAACCTTCCCTTCTTGAACCCCC AGTTATGCCAGGATTTACTAGAGAGTGTCAACTCAACCAGCAAGCGGCTCCTTCGGCTTAACTTGTGG TTGGAGGAGAACCTTTGTGGGGCTGCGTTCTCTTAGCAGTGCTCAGAAGTGACTTGCCTGAGGGTG GACCAGAAGAAGGAAAGGTCCCCTCTTGCTGTTGGCTGCACATCAGGAAGGCTGTGATGGGAATGAA AGCTGCTCTGTGTGGTGGTTAACTCCAAGAGGCAGAACTCGTTCTAGAAGGAAATGGATGCAAGCAGC TCCGGGGGCCCCAAACGCATGCTTCCTGTGGTCTAGCCCAGGGAAGCCCTTCCGTGGGGGCCCCGGCT $\tt TTGAGGGATGCCACCGGTTCTGGACGCATGGCTGATTCCTGA{\color{red}{\textbf{ATG}}} ATGATGGTTCGCCGGGGGCTGCT$ TGCGTGGATTTCCCGGGTGGTGTTTTGCTGGTGCTCCTCTGCTGTGCTATCTCTGTCCTGTACATGT TGGCCTGCACCCCAAAAGGTGACGAGGAGCAGCTGGCACTGCCCAGGGCCCAACAGCCCCACGGGGAAG GAGGGGTACCAGGCCGTCCTTCAGGAGTGGGAGGAGCAGCACCGCAACTACGTGAGCAGCCTGAAGCG GCAGATCGCACAGCTCAAGGAGGAGCTGCAGGAGGAGGAGTGAGCAGCTCAGGAATGGGCAGTACCAAG TTCCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCGTCAAGCTGGCCACAGAGTATGCAGC AGTGCCTTTCGATAGCTTTACTCTACAGAAGGTGTACCAGCTGGAGACTGGCCTTACCCGCCACCCCG AGGAGAAGCCTGTGAGGAAGGACAAGCGGGATGAGTTGGTGGAAGCCATTGAATCAGCCTTGGAGACC CTGAACAATCCTGCAGAGAACAGCCCCAATCACCGTCCTTACACGGCCTCTGATTTCATAGAAGGGAT CTACCGAACAGAAAGGGACAAAGGGACATTGTATGAGCTCACCTTCAAAGGGGACCACAAACACGAAT TCAAACGGCTCATCTTATTTCGACCATTCAGCCCCATCATGAAAGTGAAAAATGAAAAGCTCAACATG GCCAACACGCTTATCAATGTTATCGTGCCTCTAGCAAAAAGGGTGGACAAGTTCCGGCAGTTCATGCA GAATTTCAGGGAGATGTGCATTGAGCAGGATGGGAGAGTCCATCTCACTGTTGTTTACTTTGGGAAAG AAGAAATAAATGAAGTCAAAGGAATACTTGAAAACACTTCCAAAGCTGCCAACTTCAGGAACTTTACC TTCATCCAGCTGAATGGAGAATTTTCTCGGGGAAAGGGACTTGATGTTGGAGCCCGCTTCTGGAAGGG AAGCAACGTCCTTCTCTTTTTCTGTGATGTGGACATCTACTTCACATCTGAATTCCTCAATACGTGTA ATATACGGCCACCATGATGCAGTCCCTCCCTTGGAACAGCAGCTGGTCATAAAGAAGGAAACTGGATT TTGGAGAGACTTTGGATTTGGGATGACGTGTCAGTATCGGTCAGACTTCATCAATATAGGTGGGTTTG ATCTGGACATCAAAGGCTGGGGCGGAGAGGATGTGCACCTTTATCGCAAGTATCTCCACAGCAACCTC ATAGTGGTACGGACGCCTGTGCGAGGACTCTTCCACCTCTGGCATGAGAAGCGCTGCATGGACGAGCT GACCCCGAGCAGTACAAGATGTGCATGCAGTCCAAGGCCATGAACGAGGCATCCCACGGCCAGCTGG GCATGCTGGTGTTCAGGCACGAGATAGAGGCTCACCTTCGCAAACAGAAACAGAAGACAAGTAGCAAA ${\tt AAAACA} \underline{\tt TGA} {\tt ACTCCCAGAGAAGGATTGTGGGAGACACTTTTTCTTTCCTTTTGCAATTACTGAAAGTG}$ GCTGCAACAGAGAAAAGACTTCCATAAAGGACGACAAAAGAATTGGACTGATGGGTCAGAGATGAGAA AGCCTCCGATTTCTCTCTGTTGGGCTTTTTACAACAGAAATCAAAATCTCCGCTTTGCCTGCAAAAGT AACCCAGTTGCACCCTGTGAAGTGTCTGACAAAGGCAGAATGCTTGTGAGATTATAAGCCTAATGGTG TGGAGGTTTTGATGGTGTTTACAATACACTGAGACCTGTTGTTTTGTGTGCTCATTGAAATATTCATG TTATGATACTAGTGAGTACATTAAGTAAAATAAAATGGACCAGAAAAGAAAAGAAACCATAAATATCG TGTCATATTTTCCCCAAGATTAACCAAAAATAATCTGCTTATCTTTTTGGTTGTCCTTTTAACTGTCT ${\tt CCGTTTTTTTTTTTTAAAAATGCACTTTTTTTCCCTTGTGAGTTATAGTCTGCTTATTTAATTA}$ CCACTTTGCAAGCCTTACAAGAGAGCACAAGTTGGCCTACATTTTTATATTTTTTAAGAAGATACTTT GAGATGCATTATGAGAACTTTCAGTTCAAAGCATCAAATTGATGCCATATCCAAGGACATGCCAAATG CGTACAGATACTTTCTCTGAAGAGTATTTTCGAAGAGGAGCAACTGAACACTGGAGGAAAAGAAAATG ACACTTTCTGCTTTACAGAAAAGGAAACTCATTCAGACTGGTGATATCGTGATGTACCTAAAAGTCAG GTGAACCAAACAATCTCTTTTCAAAACAGGGTGCTCCTCCTGGCTTCTGGCTTCCATAAGAAGAAATG GAGAAAAATATATATATATATATATTGTGAAAGATCAATCCATCTGCCAGAATCTAGTGGGATG GAAGTTTTTGCTACATGTTATCCACCCCAGGCCAGGTGGAAGTAACTGAATTATTTTTAAATTAAGC AGTTCTACTCAATCACCAAGATGCTTCTGAAAATTGCATTTTATTACCATTTCAAACTATTTTTTAAA AATAAATACAGTTAACATAGAGTGGTTTCTTCATTCATGTGAAAATTATTAGCCAGCACCAGATGCAT GAGCTAATTATCTCTTTGAGTCCTTGCTTCTGTTTGCTCACAGTAAACTCATTGTTTAAAAGCTTCAA GAACATTCAAGCTGTTGGTGTTTAAAAAATGCATTGTATTGATTTGTACTGGTAGTTTATGAAATTT AATTAAAACACAGGCCATGAATGGAAGGTGGTATTGCACAGCTAATAAAATATGATTTGTGGATATGAA

FIGURE 276

MMMVRRGLLAWISRVVVLLVLLCCAISVLYMLACTPKGDEEQLALPRANSPTGKEGYQAVLQ
EWEEQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFL
HSQVDKAEVNAGVKLATEYAAVPFDSFTLQKVYQLETGLTRHPEEKPVRKDKRDELVEAIES
ALETLNNPAENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSPI
MKVKNEKLNMANTLINVIVPLAKRVDKFRQFMQNFREMCIEQDGRVHLTVVYFGKEEINEVK
GILENTSKAANFRNFTFIQLNGEFSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLNTCR
LNTQPGKKVFYPVLFSQYNPGIIYGHHDAVPPLEQQLVIKKETGFWRDFGFGMTCQYRSDFI
NIGGFDLDIKGWGGEDVHLYRKYLHSNLIVVRTPVRGLFHLWHEKRCMDELTPEQYKMCMQS
KAMNEASHGQLGMLVFRHEIEAHLRKQKQKTSSKKT

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FIGURE 277

 ${\tt GAAAGA} \underline{\textbf{ATG}} \texttt{TTGTGGCTGCTCTTTTTTCTGGTGACTGCCATTCATGCTGAACTCTGTCAACC}$ AGGTGCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCAT ATGCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA GTTCCCAACAGAAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGGGT ATCATTCTGGTTTGTGGTTACAGACCCTTCAAAAAATCACACCCTTCCTGCTGTTGAGGTGC CTGGAATTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTGCCCATCTG ${\tt GATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCACTACTGATTTTAT}$ CAGGGATCTGGCAACGTAGAAGAAGAACAAGAACCATCTGAAGTGGATGACGCTGAAGAT **AAGTGTGAAAACATGATCACAATTGAAAATGGCATCCCCTCTGATCCCCTGGACATGAAGGG** ${\tt GGGCATATTAATGATGCCTTCA} \underline{{\tt TGA}} {\tt CAGAGGATGAGGGCTCACCCCTCTCTGAAGGGCTGT}$ TGTTCTGCTTCCTCAAGAAATTAAACATTTGTTTCTGTGTGACTGCTGAGCATCCTGAAATA CCAAGAGCAGATCATATATTTTGTTTCACCATTCTTCTTTTGTAATAAATTTTGAATGTGCT TGAAAGTGAAAAGCAATCAATTATACCCACCAACACCACTGAAATCATAAGCTATTCACGAC TCAAAATATTCTAAAATATTTTTCTGACAGTATAGTGTATAAATGTGGTCATGTGGTATTTG ${\tt TAGTTATTGATTTAAGCATTTTTAGAAATAAGATCAGGCATATGTATATTTTCACACTTC}$ AAAGACCTAAGGAAAAATAAATTTTCCAGTGGAGAATACATATAATATGGTGTAGAAATCAT TGAAAATGGATCCTTTTTGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAG TGAGAAGTAATTATTGTAAATGGATGGATAAAAATGGAATTACTCATATACAGGGTGGAATT TTATCCTGTTATCACACCAACAGTTGATTATATATTTTCTGAATATCAGCCCCTAATAGGAC AATTCTATTTGTTGACCATTTCTACAATTTGTAAAAGTCCAATCTGTGCTAACTTAATAAAG

FIGURE 278

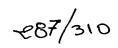
MLWLLFFLVTAIHAELCQPGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVP NREATEISHVLLCNVTQRVSFWFVVTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTLE FLKIPSTLAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRRKNKEPSEVDDAEDKC ENMITIENGIPSDPLDMKGGILMMPS

ATGGCAAGAGCTCTACTCGTGCGGTGCTTCTTCTCCTTGGCATACAGCTCACAGCTCTTTGG CCTATAGCAGCTGTGGAAATTTATACCTCCCGGGTGCTGGAGGCTGTTAATGGGACAGATGC TCGGTTAAAATGCACTTTCTCCAGCTTTGCCCCTGTGGGTGATGCTCTAACAGTGACCTGGA ATTTTCGTCCTCTAGACGGGGACCTGAGCAGTTTGTATTCTACTACCACATAGATCCCTTC CAACCCATGAGTGGGCGGTTTAAGGACCGGGTGTCTTGGGATGGGAATCCTGAGCGGTACGA TGCCTCCATCCTTCTCTGGAAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGA AGAACCCACCTGATGTTGATGGGGTGATAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTA $\tt CGCTTCTCTGAGATCCACTTCCTGGCTCTGGCCATTGGCTCTGCCTGTGCACTGATGATCAT$ AATAGTAATTGTAGTGGTCCTCTTCCAGCATTACCGGAAAAAGCGATGGGCCGAAAGAGCTC ATAAAGTGGTGGAGATAAAATCAAAAGAAGAGGGAAAGGCTCAACCAAGAGAAAAAGGTCTCT ${\tt GTTTATTTAGAAGACACAGAC} {\tt TAA} {\tt CAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAA}$ ${\tt GAACCCTAGTATTCTTGAAGTTAATGGAAACTTTTCTTTGGCTTTTCCAGTTGTGACCCGT}$ AGTGCTCCTCCATATCACCAGTCATACACAGCCTCATTATTAAGGTCTTATTTAATTTCAGA GTGTAAATTTTTTCAAGTGCTCATTAGGTTTTATAAACAAGAAGCTACATTTTTGCCCTTAA GACACTACTTACAGTGTTATGACTTGTATACACATATATTGGTATCAAAGGGGATAAAAGCC ${\tt AATTTGTCTGTTACATTTCCTTTCACGTATTTCTTTTAGCAGCACTTCTGCTACTAAAGTTA}$ ATGTGTTTACTCTCTTCCCTCCCACATTCTCAATTAAAAGGTGAGCTAAGCCTCCTCGGTG ${\tt TTTCTGATTAACAGTAAATCCTAAATTCAAACTGTTAAATGACATTTTTATTTTTATGTCTC}$ TTTGTCG

FIGURE 280

MYGKSSTRAVLLLLGIQLTALWPIAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTVT
WNFRPLDGGPEQFVFYYHIDPFQPMSGRFKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQ
VKNPPDVDGVIGEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVIVVVLFQHYRKKRWAER
AHKVVEIKSKEEERLNQEKKVSVYLEDTD

 ${\tt MKFLAVLVLLGVSIFLVSAQNPTTAAPADTYPATGPADDEAPDAETTAAATTATTAAPTTAT}$ ${\tt TAASTTARKDIPVLPKWVGDLPNGRVCP}$



 ${\tt MLPPALPPALVFTVAWSLLAERVSWVRDAEDAHRLQPFVTERTLGKVQRWSGVHTQTGGRAG}\\ {\tt GGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLLCCWPVGVARGGALCQ}$

FIGURE 285

FIGURE 286

MPVPALCLLWALAMVTRPASAAPMGGPELAQHEELTLLFHGTLQLGQALNGVYRTTEGRLTK
ARNSLGLYGRTIELLGQEVSRGRDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQK
VLRDSVQRLEVQLRSAWLGPAYREFEVLKAHADKQSHILWALTGHVQRQRREMVAQQHRLRQ
IQERLHTAALPA

FIGURE 287

 ${\tt GGCAAC} \underline{\textbf{ATG}} {\tt GCTCAGCAGGCTTGCCCCAGAGCCATGGCAAAGAATGGACTTGTAATTTGCAT}$ ${\tt CCTGGTGATCACCTTACTCCTGGACCAGACCACCAGCCACACATCCAGATTAAAAGCCAGGA}$ AGCACAGCAAACGTCGAGTGAGAGACAAGGATGGAGATCTGAAGACTCAAATTGAAAAGCTC TAAAGTTCACAAGAAATGCTACCTTGCTTCAGAAGGTTTGAAGCATTTCCATGAGGCCAATG AAGACTGCATTTCCAAAGGAGGAATCCTGGTTATCCCCAGGAACTCCGACGAAATCAACGCC ${\tt CATGGTCACGGAAGGCAAGTTTGTTGACGTCAACGGAATCGCTATCTCCTTCAACTGGG}$ ACCGTGCACAGCCTAACGGTGGCAAGCGAGAAAACTGTGTCCTGTTCTCCCAATCAGCTCAG GGCAAGTGGAGTGATGAGGCCTGTCGCAGCAGCAAGAGATACATATGCGAGTTCACCATCCC ${ t TAAA} { t TAG} { t GTCTTTCTCCAATGTGTCCTCCAAGCAAGATTCATCATAACTTATAGGTTCATGA$ TCTCTAAGATCAAGTAAAATCATAATTTTTACTTATTAAAAAATTGCAACACAAGATCAAT GTCCATAGCAATATGATAGCATCAGCCAATTTTGCTAACACATTTCTTTGGGATTTTGCCCT TCCTGGGGTATAGGGGATCAGAAATATTGATCCATGTGCACGCAGATAAAATGGCTTCTGCT ${\tt TTCCCTTGGAAGTTTAGCGTATGTTTGACTAACAAAAATTCCCTACATCAGAGACTCTAGGT}$ GCTATATAATCCAAAAACTTTTCAGCCTGTTGCTCATTCTGTCCCATGCTGGCAATAATACC ${\tt TTGTCAGCCCATTACCCTTATTTTGAATTGCTCCATCTCCTGGTGGGACTTGTATCTTGTCT}$ TACCCTTTTTTTGGAAGTTTCCAGCCGCAATTTGAAATGAAATGACAAGGTGTATATTTGAT CAATTTCATTCCCACCATTGCATTACAACCTCTAACTTAAATGGGTAACCCTAAGGCATAT ${\tt AGCATCCTTACTCTCACCTTTTATGAGATTGAGAGTGGACTTACATTTCCTTTTTTACATTT}$ TCGTATATTTATTTTTTTAGCCATCATTATATGTTTAAGTCTATTATGGGCAACCAATCTT TGGAAGCTGAAAACTGAATTTAAAGAATGCTATCTTGGAAAATTGCATACGTCTGTGCAATT TTTTATTCTGCCTAGTGCTATTCTGCTTGTTTAACTAGATTGTACAAAATAACTTCATTGCT TAATATCAAATTACAAAGTTTAGACTTGGAGGGAAATGGGCTTTTTAGAAGCAAACAATTTT AAATATATTTTGTTCTTCAAATAAATAGTGTTTAAACATTGAATGTGTTTTGTGAACAATAT CCCACTTTGCAAACTTTAACTACACATGCTTGGAATTAAGTTTTAGCTGTTTTCATTGCTCA

MAQQACPRAMAKNGLVICILVITLLLDQTTSHTSRLKARKHSKRRVRDKDGDLKTQIEKLWT EVNALKEIQALQTVCLRGTKVHKKCYLASEGLKHFHEANEDCISKGGILVIPRNSDEINALQ DYGKRSLPGVNDFWLGINDMVTEGKFVDVNGIAISFLNWDRAQPNGGKRENCVLFSQSAQGK WSDEACRSSKRYICEFTIPK

২৪/১। ০ FIGURE 289

FIGURE 290

 ${\tt MKLAALLGLCVALSCSSAAAFLVGSAKPVAQPVAALESAAEAGAGTLANPLGTLNPLKLLLS} \\ {\tt SLGIPVNHLIEGSQKCVAELGPQAVGAVKALKALLGALTVFG}$

PCT/US99/12252

FIGURE 291

TGAAGGACTTTTCCAGGACCCAAGGCCACACACTGGAAGTCTTGCAGCTGAAGGGAGGCACT GCACAGGTGTGGCTGGTACCCGGCTTGGCCCCAGTCCTCAGTCGCCAGAGACCCCAGCCCC TCAGAACCAGACCAGCAGGTAGTGCAGGCTCCCAGGGAGGAAGAGAAGATGAGCAGGAGG ${\tt CCAGCGAGGAGAAGGCCGGTGAGGAAGAGACCTGGCTGATGGCCAGCAGCAGCAGCTT}$ GCCAAGGAGACTTCAAACTTCGGATTCAGCCTGCTGCGAAAGATCTCCATGAGGCACGATGG CAGGGCCGACTGAAACCCAGATCAAGAGAGGGGCTCCACTTGCAGGCCCTGAAGCCCACCAAG CCCGGGCTCCTGCCTCTTTAAGGGACTCAGAGAGACCCTCTCCCGCAACCTGGAACT GGGCCTCTCACAGGGGAGTTTTGCCTTCATCCACAAGGATTTTGATGTCAAAGAGACTTTCT TCAATTTATCCAAGAGGTATTTTGATACAGAGTGCGTGCCTATGAATTTTCGCAATGCCTCA CAGGCCAAAAGGCTCATGAATCATTACATTAACAAAGAGACTCGGGGGAAAATTCCCAAACT GTTTGATGAGATTAATCCTGAAACCAAATTAATTCTTGTGGATTACATCTTGTTCAAAGGGA AATGGTTGACCCCATTTGACCCTGTCTTCACCGAAGTCGACACTTTCCACCTGGACAAGTAC AAGACCATTAAGGTGCCCATGATGTACGGTGCAGGCAAGTTTGCCTCCACCTTTGACAAGAA ${\tt TTTTCGTTGTCATGTCCTCAAACTGCCCTACCAAGGAAATGCCACCATGCTGGTGGTCCTCA}$ TGGAGAAAATGGGTGACCACCTCGCCCTTGAAGACTACCTGACCACAGACTTGGTGGAGACA ${\tt GAAGTATGAGATGCATGAGCTGCTTAGGCAGATGGGAATCAGAAGAATCTTCTCACCCTTTG}$ $\tt CTGACCTTAGTGAACTCTCAGCTACTGGAAGAATCTCCAAGTATCCAGGGTTTTACGAAGA$ ACAGTGATTGAAGTTGAAAAGGGGCACTGAGGCAGTGGCAGGAATCTTGTCAGAAATTAC TGCTTATTCCATGCCTCCTGTCATCAAAGTGGACCGGCCATTTCATTTCATGATCTATGAAG ${\tt AAACCTCTGGAATGCTTCTGTTTCTGGGCAGGGTGGTGAATCCGACTCTCCTA} \underline{{\tt TAA}} {\tt TTCAGG}$ AAATAAATACAGTAGTCCCCACTTATCTGAGGGGGATACATTCAAAGACCCCCAGCAGATGC AAAGTTTAATTTATAAATTAGGCACAGTAAGAGATTAACAATAATAACAACATTAAGTAAAA TGAGTTACTTGAACGCAAGCACTGCAATACCATAACAGTCAAACTGATTATAGAGAAGGCTA ${\tt CATCCTGGGTGGGACAGAGCGATGCAAGATTCCATCCCACTACTCAGAATGGCATGC}$ ${\tt TGCTTAAGACTTTTAGATTGTTTATTTCTGGAATTTTTCATTTAATGTTTTTGGACCATGGT}$ TGACCATGGTTAACTGAGACTGCAGAAAGCAAAACCATGGATAAGGGAGGACTACTACAAAA

FIGURE 292

MKVVPSLLLSVLLAQVWLVPGLAPSPQSPETPAPQNQTSRVVQAPREEEEDEQEASEEKAGE
EEKAWLMASRQQLAKETSNFGFSLLRKISMRHDGNMVFSPFGMSLAMTGLMLGATGPTETQI
KRGLHLQALKPTKPGLLPSLFKGLRETLSRNLELGLSQGSFAFIHKDFDVKETFFNLSKRYF
DTECVPMNFRNASQAKRLMNHYINKETRGKIPKLFDEINPETKLILVDYILFKGKWLTPFDP
VFTEVDTFHLDKYKTIKVPMMYGAGKFASTFDKNFRCHVLKLPYQGNATMLVVLMEKMGDHL
ALEDYLTTDLVETWLRNMKTRNMEVFFPKFKLDQKYEMHELLRQMGIRRIFSPFADLSELSA
TGRNLQVSRVLRRTVIEVDERGTEAVAGILSEITAYSMPPVIKVDRPFHFMIYEETSGMLLF
LGRVVNPTLL

২৭7/310 FIGURE 293

≈38/310 FIGURE 294

MRRLLLVTSLVVVLLWEAGAVPAPKVPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVL FPVQKPKLLTTEEKPRGQGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEE RPRLWVMPNHQVLLGPEEDQDHIYHPQ

FIGURE 295

 ${\tt TACCCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACA} \underline{{\tt ATG}} {\tt AACCAACTCAGCTTCCTGC}$ TGGACCTGTTCTTCGTCTCCATCTCTGCCCAGAAGCTGCAAGGAAATCAAAGACGAATGTCC TAGTGCATTTGATGGCCTGTATTTTCTCCGCACTGAGAATGGTGTTATCTACCAGACCTTCT GTGACATGACCTCTGGGGGTGGCGGCTGGACCCTGGTGCCAGCGTGCATGAGAATGACATG ${\tt CGTGGGAAGTGCACGGTGGGCGATCGCTGGTCAGTCAGCAGGGCAGCAAAGCAGACTACCC}$ AGAGGGGGACGCCAACTACAACACCTTTGGATCTGCAGAGGCGGCCACGAGCG ATGACTACAAGAACCCTGGCTACTACGACATCCAGGCCAAGGACCTGGGCATCTGGCACGTG CCCAATAAGTCCCCCATGCAGCACTGGAGAAACAGCTCCCTGCTGAGGTACCGCACGGACAC TGGCTTCCTCCAGACACTGGGACATAATCTGTTTGGCATCTACCAGAAATATCCAGTGAAAT ${\tt ATGGAGAAGGAAAGTGTTGGACTGACAACGGCCCGGTGATCCCTGTGGTCTATGATTTTGGC}$ GACGCCCAGAAAACAGCATCTTATTACTCACCCTATGGCCAGCGGGAATTCACTGCGGGATT TGTTCAGTTCAGGGTATTTAATAACGAGAGAGCCAGCCCAACGCCTTGTGTGCTGGAATGAGGG ${\tt TCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAGGATACTTTCCAGAGGCCAGT}$ ${\tt CCCCAGCAGTGTGGAGATTTTCTGGTTTGATTGGAGTGGATATGGAACTCATGTTGGTTA}$ ${\tt CAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCGT} \underline{{\tt TGA}}{\tt GAGTTTTGTG}$ GGAGGGAACCCAGACCTCCCCCAACCATGAGATCCCAAGGATGGAGAACAACTTACCCA GTAGCTAGAATGTTAATGGCAGAAGAGAAAAACAATAAATCATATTGACTCAAGAAAAAAA

FIGURE 296

MNQLSFLLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTEN
GVIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANYNTFG
SAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLGHNLFGI
YQKYPVKYGEGKCWTDNGPVIPVVYDFGDAQKTASYYSPYGQREFTAGFVQFRVFNNERAAN
ALCAGMRVTGCNTEHHCIGGGGYFPEASPQQCGDFSGFDWSGYGTHVGYSSSREITEAAVLLFYR

FIGURE 297

GCGGAGCCGGCCGGCTGCGCAGAGGAGCCGCTCTCGCCGCCGCCACCTCGGCTGGGAGCC ${\tt CACGAGGCTGCCGCATCCTGCCCTCGGAACA}$ CGCTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGCTGGGGGCCCCCATGAAAGCGCAGCC ATGGCGGCATCTGCAAACATAGAGAATTCTGGGCTTCCACACAACTCCAGTGCTAACTCAAC AGAGACTCTCCAACATGTGCCTTCTGACCATACAAATGAAACTTCCAACAGTACTGTGAAAC CACCAACTTCAGTTGCCTCAGACTCCAGTAATACAACGGTCACCACCATGAAACCTACAGCG GCATCTAATACAACAACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTTAAAGTC TACACCCAAAACAACAAGTGTTTCACAGAACACATCTCAGATATCAACATCCACAATGACCG TAACCCACAATAGTTCAGTGACATCTGCTGCTTCATCAGTAACAATCACAACAACTATGCAT TCTGAAGCAAAGAAAGGATCAAAATTTGATACTGGGAGCTTTGTTGGTGGTATTGTATTAAC GCTGGGAGTTTTATCTATTCTTTACATTGGATGCAAAATGTATTACTCAAGAAGAGGCATTC ${\tt GGTATCGAACCATAGATGAACATGATGCCATCATT} \underline{{\tt TAA}} {\tt GGAAATCCATGGACCAAGGATGGA}$ ATACAGATTGATGCTGCCCTATCAATTAATTTTGGTTTATTAATAGTTTAAAACAATATTCT CTTTTTGAAAATAGTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTA AAGATTCTTCAAGGTAACAAGGGTTTGGGGTTTTGAAATAAACATCTGGATCTTATAGACCGT GGGGTGGGGGCATTGGTCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAA TGCCATCTGGGCATACAAATAAGAAGTTTGTCACAGCACTCAGGATTTTGGGTATCTTTTGT AGCTCACATAAAGAACTTCAGTGCTTTTCAGAGCTGGATATATCTTAATTACTAATGCCACA CAGAAATTATACAATCAAACTAGATCTGAAGCATAATTTAAGAAAAACATCAACATTTTTTG TGCTTTAAACTGTAGTAGTTGGTCTAGAAACAAAATACTCC

FIGURE 298

MGLGARGAWAALLLGTLQVLALLGAAHESAAMAASANIENSGLPHNSSANSTETLQHVPSDH TNETSNSTVKPPTSVASDSSNTTVTTMKPTAASNTTTPGMVSTNMTSTTLKSTPKTTSVSQN TSQISTSTMTVTHNSSVTSAASSVTITTTMHSEAKKGSKFDTGSFVGGIVLTLGVLSILYIG CKMYYSRRGIRYRTIDEHDAII

FIGURE 299

CAGCCGGGTCCCAAGCCTGTGCCTGAGCCTGAGCCTGAGCCCGAGCCGGGAGCCGG ${\tt TCGCGGGGCTCCGGGCTGTGGGACCGCTGGGCCCCCAGCG} {\tt ATG} {\tt GCGACCCTGTGGGGAGGC}$ ${\tt ATAAAGAAAATTCTGGGCATATTTATAATAAGAACATATCTCAGAAAGATTGTGATTGCCTT}$ CATGTTGTGGAGCCCATGCCTGTGCGGGGGCCTGATGTAGAAGCATACTGTCTACGCTGTGA ATGCAAATATGAAGAAGAAGCTCTGTCACAATCAAGGTTACCATTATAATTTATCTCTCCA TTTTGGGCCTTCTACTTCTGTACATGGTATATCTTACTCTGGTTGAGCCCATACTGAAGAGG ${\tt CGCCTCTTTGGACATGCACAGTTGATACAGAGTGATGATATTGGGGATCACCAGCCTTT}$ TGCAAATGCACACGATGTGCTAGCCCGCTCCCGCAGTCGAGCCAACGTGCTGAACAAGGTAG ${\tt CATGTTGTCCTCAGC} \underline{{\tt TAA}} {\tt TTGGGAATTGAATTCAAGGTGACTAGAAAGAAACAGGCAGACAA}$ CTGGAAAGAACTGACTGGGTTTTGCTGGGTTTCATTTTAATACCTTGTTGATTTCACCAACT ATAATAGAGACATTTTTAAAAGCACACAGCTCAAAGTCAGCCAATAAGTCTTTTCCTATTTG TGACTTTTACTAATAAAATAAATCTGCCTGTAAATTATCTTGAAGTCCTTTACCTGGAACA ${\tt AGCACTCTTTTTCACCACATAGTTTTAACTTGACTTTCAAGATAATTTTCAGGGTTTTTG}$ AACAACTTTTTCAAGTCACTTTACTAAACAAACTTTTGTAAATAGACCTTACCTTCTATTT TCGAGTTTCATTTATATTTTGCAGTGTAGCCAGCCTCATCAAAGAGCTGACTTACTCATTTG ACTTTTGCACTGACTGTATTATCTGGGTATCTGCTGTGTCTGCACTTCATGGTAAACGGGAT ${\tt CTAAAATGCCTGGTGGCTTTTCACAAAAAGCAGATTTTCTTCATGTACTGTGATGTCTGATG}$ CAATGCATCCTAGAACAAACTGGCCATTTGCTAGTTTACTCTAAAGACTAAACATAGTCTTG ${\tt GTGTGTGTGTCTTACTCATCTTCTAGTACCTTTAAGGACAAATCCTAAGGACTTGGACACT}$ TGCAATAAAGAAATTTTATTTTAAACCCAAGCCTCCCTGGATTGATAATATATACACATTTG TCAGCATTTCCGGTCGTGGTGAGAGGCAGCTGTTTGAGCTCCAATATGTGCAGCTTTGAACT ${\tt AGGGCTGGGGTTGTGGGTGCCTCTTCTGAAAGGTCTAACCATTATTGGATAACTGGCTTTTT}$ TCTTCCTATGTCCTCTTTGGAATGTAACAATAAAAATAATTTTTGAAACATCAA

FIGURE 300

MATLWGGLLRLGSLLSLSCLALSVLLLAQLSDAAKNFEDVRCKCICPPYKENSGHIYNKNIS QKDCDCLHVVEPMPVRGPDVEAYCLRCECKYEERSSVTIKVTIIIYLSILGLLLLYMVYLTL VEPILKRRLFGHAQLIQSDDDIGDHQPFANAHDVLARSRSRANVLNKVEYAQQRWKLQVQEQ RKSVFDRHVVLS

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FIGURE 302

MAYSTVQRVALASGLVLALSLLLPKAFLSRGKRQEPPPTPEGKLGRFPPMMHHHQAPSDGQT PGARFQRSHLAEAFAKAKGSGGGAGGGGSGRGLMGQIIPIYGFGIFLYILYILFKVSRIILI ILHQ

FIGURE 303

 $\tt CGGCTCGAGTGCAGCTGTGGGAGATTTCAGTGCATTGCCTCCCCTGGGTGCTCTTCATCTT$ ${\tt GGATTTGAAAGTTGAGAGCAGC}$ TGGATTATTCCTTGGGCCTGAATGACTTGAATGTTTCCCCGCCTGAGCTAACAGTCCATGTG GGTGATTCAGCTCTGATGGGATGTGTTTTCCAGAGCACAGAAGACAAATGTATATTCAAGAT ${\tt AGACTGGACTCTGTCACCAGGAGGAGGACGCCAAGGACGAATATGTGCTATACTATTACTCCA}$ ${\tt ATCTCAGTGTGCCTATTGGGCGCTTCCAGAACCGCGTACACTTGATGGGGGACATCTTATGC}$ AATGATGGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGA AATCCGCCTCAAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGGTACTGCATGTGCTTCCAG AGCACAGAAGTGAAACACGTGACCAAGGTAGAATGGATATTTTCAGGACGGCGCGCAAAGGA GGAGATTGTATTTCGTTACTACCACAAACTCAGGATGTCTGTGGAGTACTCCCAGAGCTGGG GCCACTTCCAGAATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCATCATG CTTCAAGGAGTGAGGGAGTCAGATGGAGGAAACTACACCTGCAGTATCCACCTAGGGAACCT GGTGTTCAAGAAAACCATTGTGCTGCATGTCAGCCCGGAAGAGCCCTCGAACACTGGTGACCC ${\tt CGGCAGCCCTGAGGCCTCTGGTCTTGGGTGATCAGTTGGTGATCATTGTGGGAATTGTC}$ TGTGCCACAATCCTGCTGCTCCCTGTTCTGATATTGATCGTGAAGAAGACCTGTGGAAATAA GAGTTCAGTGAATTCTACAGTCTTGGTGAAGAACACGAAGAAGACTAATCCAGAGATAAAAG AAAAACCCTGCCATTTTGAAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATAATTGTA ${\tt CGGGAGGTGATCGAGGAAAAAATCAGAGGCCACCTACATGACCATGCA}$ ${\tt GAATGCCAAAAACACAGCAAGCCTTT}$ TGGAGACTCTCTCTGTGTGTGTCCTGGGCCACTCTACCAGTGATTTCAGACTCCCGCTCTC CCAGCTGTCCCCTGTCTCATTGTTTGGTCAATACACTGAAGATGGAGAATTTGGAGCCTGG ${\tt CAGAGAGACTGGAGGGGAGGGAGGGAGGGAGGGAGCATGGACTTGGC}$ $\tt CTCTGGAGTGGGACACTGGCCTGGGAACCAGGCTGAGTGGCCTCAAACCCCCCGTT$ GGATCAGACCCTCCTGTGGGCAGGGTTCTTAGTGGATGAGTTACTGGGAAGAATCAGAGATA AAAACCAACCCAAATCAA

FIGURE 304

MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLSPG
EHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLKGES
QVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYY
HKLRMSVEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGNLVFKKTIV
LHVSPEEPRTLVTPAALRPLVLGGNQLVIIVGIVCATILLLPVLILIVKKTCGNKSSVNSTV
LVKNTKKTNPEIKEKPCHFERCEGEKHIYSPIIVREVIEEEEPSEKSEATYMTMHPVWPSLR
SDRNNSLEKKSGGGMPKTQQAF

309/310 FIGURE 305

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAAATGTGTCCCATCTCACATG GTTCTACCCTACTAAAGACAGGAAGATCATAAACTGACAGATACTGAAATTGTAAGAGTTGG ${\tt AAACTACATTTTGCAAAGTCATTGAACTCTGAGCTCAGTTGCAGTACTCGGGAAGCC} \underline{{\tt ATG}CA}$ GGATGAAGATGGATACATCACCTTAAATATTAAAACTCGGAAACCAGCTCTCGTCTCCGTTG ATGGTTGTCGGGCTGGTGGCTCTGGGGATTTGGTCTGTCATGCAGCGCAATTACCTACAAGA TGAGAATGAAAATCGCACAGGAACTCTGCAACAATTAGCAAAGCGCTTCTGTCAATATGTGG TAAAACAATCAGAACTAAAGGGCACTTTCAAAGGTCATAAATGCAGCCCCTGTGACACAAAC TGGAGATATTATGGAGATAGCTGCTATGGGTTCTTCAGGCACAACTTAACATGGGAAGAGAG ${\tt TAAGCAGTACTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGG}$ ${\tt AGTACATCAAAGCCAGGACTCATTTAATTCGTTGGGTCGGATTATCTCGCCAGAAGTCGAAT}$ ${\tt GAGGTCTGGAAGTGGGAGGATGGCTCGGTTATCTCAGAAAATATGTTTGAGTTTTTGGAAGA}$ TGGAAAAGGAAATATGAATTGTGCTTATTTTCATAATGGGAAAATGCACCCTACCTTCTGTG AGAACAAACATTATTTAATGTGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT ${\color{red}{\bf TAA}}$ TGCAAAGAGGTGGACAGGATAACACAGATAAGGGCTTTATTGTACAATAAAAGATATGT ATGAATGCATCAGTAGCTGAAAAAAAAAAAAA

FIGURE 306

MQDEDGYITLNIKTRKPALVSVGPASSSWWRVMALILLILCVGMVVGLVALGIWSVMQRNYL QDENENRTGTLQQLAKRFCQYVVKQSELKGTFKGHKCSPCDTNWRYYGDSCYGFFRHNLTWE ESKQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMFEFL EDGKGNMNCAYFHNGKMHPTFCENKHYLMCERKAGMTKVDQLP

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(30) 60/088,810	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,355	23 Jun/juin 1998 (23.06.1998)	US	(30) 60/091,626	2 Jul/juil 1998 (02.07.1998)	US
(30) 60/088,811	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,349	23 Jun/juin 1998 (23.06.1998)	US	(30) 60/091,628	2 Jul/juil 1998 (02.07.1998)	US
(30) 60/088,824	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,429	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,633	2 Jul/juil 1998 (02.07.1998)	US
(30) 60/088,825	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,431	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,646	2 Jul/juil 1998 (02.07.1998)	US
(30) 60/088,826	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,435	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,673	2 Jul/juil 1998 (02,07,1998)	us
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(30) 60/088,861	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,445	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,982	7 Jul/juil 1998 (07.07.1998)	us
(30) 60/088,863	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,461	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/092,182	9 Jul/juil 1998 (09.07.1998)	US
(30) 60/088,876	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,472	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/092,472	10 Jul/juil 1998 (10.07.1998)	US
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(30) 60/089,105	12 Jun/juin 1998 (12.06.1998)	US	(30) 60/090,538	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/094,651	30 Jul/juil 1998 (30.07.1998)	US
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(30) 60/089,512	16 Jun/juin 1998 (16.06.1998)	US	(30) 60/090,557	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/095,285	4 Aug/août 1998 (04.08.1998)	US
(30) 60/089,514	16 Jun/juin 1998 (16.06.1998)	US	(30) 60/090,676	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,301	4 Aug/août 1998 (04.08.1998)	US
(30) 60/089,532	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,678	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,302	4 Aug/août 1998 (04.08.1998)	US
(30) 60/089,538	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,688	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,318	4 Aug/août 1998 (04.08.1998)	US
(30) 60/089,598	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,690	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,321	4 Aug/août 1998 (04.08.1998)	US
(30) 60/089,599	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,691	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,325	4 Aug/août 1998 (04.08.1998)	US .
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(30) 60/089,653	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,695	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,929	10 Aug/août 1998 (10.08.1998)	US
(30) 60/089,801	18 Jun/juin 1998 (18.06.1998)	US	(30) 60/090,696	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/096,012	10 Aug/août 1998 (10.08.1998)	US
(30) 60/089,907	18 Jun/juin 1998 (18.06.1998)	US	(30) 60/090,862	26 Jun/juin 1998 (26.06.1998)	us	(30) 60/096,143 (30) 60/096,146	11 Aug/août 1998 (11.08.1998)	US
(30) 60/089,908	18 Jun/juin 1998 (18.06.1998)	US	(30) 60/090,863	26 Jun/juin 1998 (26.06.1998)	US	(30) 60/096,329	11 Aug/août 1998 (11.08.1998) 12 Aug/août 1998	US
(30) 60/089,947	19 Jun/juin 1998 (19.06.1998)	US	(30) 60/091,358	1 Jul/juil 1998 (01.07.1998)	US	(30) 60/096,757	(12.08.1998) 17 Aug/août 1998	US
(30) 60/089,948	19 Jun/juin 1998 (19.06.1998)	US	(30) 60/091,360	1 Jul/juil 1998 (01.07.1998)	US	(30) 60/096,766	(17.08.1998) 17 Aug/eoût 1998	US
(30) 60/089,952	19 Jun/juin 1998 (19.06.1998)	US	(30) 60/091,544	1 Jul/juil 1998 (01.07.19 98)	US	(30) 60/096,768	(17.08.1998) 17 Aug/août 1998	US
(30) 60/090,246	22 Jun/juin 1998 (22.06.1998)	US	(30) 60/091,486	2 Jul/juli 1998 (02.07.1998)	US	(30) 60/096,773	(17.08.1998) 17 Ang/août 1998	US
(30) 60/090,252	22 Jun/juin 1998 (22.06.1998)	บร	(30) 60/091,519	2 Jul/juil 1998 (02.07.1998)	US	(30) 60/096,791	(17.08.1998) 17 Aug/août 1998	US
				((17.08.1998)	

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(30) 60/096,891	17 Ang/août 1998 (17.08.1998)	US
(30) 60/096,894	17 Aug/août 1998 (17.08.1998)	US
(30) 60/096,895	17 Aug/août 1998 (17.08.1998)	US
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(30) 60/096,950	18 Aug/août 1998 (18.08.1998)	US
(30) 60/096,959	18 Aug/août 1998 (18.08.1998)	US
(30) 60/096,960	18 Aug/août 1998 (18.08.1998)	US
(30) 60/097,022	18 Aug/août 1998 (18.08.1998)	US
(30) 60/097,141	19 Aug/août 1998 (19.08.1998)	US
(30) 60/097,218	20 Aug/août 1998 (20.08.1998)	US
(30) 60/097,661	24 Aug/août 1998 (24.08.1998)	US
(30) 60/097,951	26 Aug/août 1998 (26.08.1998)	US
(30) 60/097,952	26 Aug/août 1998 (26.08.1998)	US
(30) 60/097,954	26 Aug/août 1998 (26.08.1998)	US
(30) 60/097,955	26 Aug/août 1998 (26.08.1998)	US
(30) 60/097,971	26 Aug/août 1998 (26.08.1998)	US
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(30) 60/097,979	26 Aug/août 1998 (26.08.1998)	US
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(30) 60/098,014	26 Aug/août 1998 (26.08.1998)	US
(30) 60/098,525	31 Aug/soût 1998 (31.08.1998)	US
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		60/087,827	3 June 1998 (03.06.1998	3) US	60/090,254	22 June 1998 (22.06.1998)	US
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=		60/088,167	5 June 1998 (05.06.1998	,		24 June 1998 (24.06.1998)	US
=		60/088,202	5 June 1998 (05.06.1998		60/090,472	24 June 1998 (24.06.1998)	US
≡		60/088,212	5 June 1998 (05.06.1998			24 June 1998 (24.06.1998)	US
		60/088,217	5 June 1998 (05.06.1998		60/090,538	24 June 1998 (24.06.1998)	US
		60/088,655	9 June 1998 (09.06.1998		60/090,540	24 June 1998 (24.06.1998)	US
		60/088,722	10 June 1998 (10.06.1998		60/090,557	24 June 1998 (24.06.1998)	US
≣		60/088,730	10 June 1998 (10.06.1998	•	60/090,676	25 June 1998 (25.06.1998)	US
≣		60/088,734	10 June 1998 (10.06.1998		60/090,678	25 June 1998 (25.06.1998)	US
Ξ		60/088,738	10 June 1998 (10.06.1998		60/090,688	25 June 1998 (25.06.1998)	US.
Ξ		60/088,740	10 June 1998 (10.06.1998		60/090,690	25 June 1998 (25.06.1998)	US
≣		60/088,741	10 June 1998 (10.06.1998		60/090,691	25 June 1998 (25.06.1998)	US
Ξ		60/088,742	10 June 1998 (10.06.1998	•	60/090,694	25 June 1998 (25.06.1998)	US
≣		60/088,810	10 June 1998 (10.06.1998		60/090,695	25 June 1998 (25.06.1998)	US
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≣		60/088,824	10 June 1998 (10.06.1998		60/090,862	26 June 1998 (26.06.1998)	US
Ξ		60/088,825	10 June 1998 (10.06.1998		60/090,863	26 June 1998 (26.06.1998)	US
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≡		60/088,858	11 June 1998 (11.06.1998	•	60/091,360	1 July 1998 (01.07.1998)	US
≣		60/088,861	11 June 1998 (11.06.1998	•	60/091,544	1 July 1998 (01.07.1998)	US
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_						[Communed on next]	- Bel

O 99/63088 A3

⁽⁵⁴⁾ Title: MEMBRANE-BOUND PROTEINS AND NUCLEIC ACIDS ENCODING THE SAME

⁽⁵⁷⁾ Abstract: The present invention is directed to membrane-bound polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.



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60/097,218	20 August 1998 (20.08.1998)	US
60/097,661	24 August 1998 (24.08.1998)	US
60/097,951	26 August 1998 (26.08.1998)	US
60/097,952	26 August 1998 (26.08.1998)	US
60/097,954	26 August 1998 (26.08.1998)	US
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60/097,978	26 August 1998 (26.08.1998)	US
60/097,979	26 August 1998 (26.08.1998)	US
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60/098,525	31 August 1998 (31.08.1998)	US
60/100,634	16 September 1998 (16.09.1998)	US
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- (74) Agents: KRESNAK, Mark, T. et al.; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US).
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- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERITIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER 1PC 6 C12N15/12 C07K14/705 C12N15/62 C07K16/28 According to International Patent Classification (IPC) or to both national classification and IPC 8. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) 1PC 6 C12N C07K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Catagory* Clastion of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X HILLIER ET AL.: "The WashU-Merck EST Project." EMBL DATABASE ENTRY HSAA150370; ACCESSION NUMBER AA150370, 15 December 1996 (1996-12-15), XP002125640 abstract X STRAUSBERG R.: "NCI, Cancer genome Anatomy Project." EMBL DATABASE ENTRY AA865629; ACCESSION NUMBER AA865629, 16 March 1998 (1998-03-16), XP002125641 abstract -/
B. FIELDS SEARCHED Minutural documentation searched (classification system followed by classification symbols) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category* Clation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X HILLIER ET AL.: "The WashU-Merck EST
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Anatomy Project." EMBL DATABASE ENTRY AA865629; ACCESSION NUMBER AA865629, 16 March 1998 (1998-03-16), XP002125641 abstract -/
Further documents are listed in the continuation of box C.
A document defining the general state of the art which is not considered to be of particular relevance "E* earlier document but published on or after the international filing date "C* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O' document referring to an oral disclosure, use, exhibition or other means "T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone cannot be considered to involve an inventive step when the document is combined with one or more other such document is combined with one or more other such document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is taken alone cannot be considered to involve an inventive step when the document is combined with one or more other such document is combined with one or more other such document such document is combined with one or more other such document such d
*P' document published prior to the international filing date but later than the pnority date claimed "&" document member of the same patent family
Date of the actual completion of the international search Date of mailing of the international search report 20 December 1999
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Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk. Tel (+31-70) 340-3016 Fax: (+31-70) 340-3016 Mand] B

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C.(Continua Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	
	Common of coccurrent, with indecautin, where appropriate, or the relevant passages	Relevant to claim No.
X .	STRAUSBERG R.: "NCI Cancer Genome Anatomy Project." EMBL DATABASE ENTRY AA843667; ACCESSION NUMBER AA843667, 10 March 1998 (1998-03-10), XP002125642 abstract	1-13,21, 22
P,X	WO 98 39448 A (HUMAN GENOME SCIENCES) 11 September 1998 (1998-09-11) page 413 page 531 -page 532 page 647 -page 648	1-13, 17-26
P,X	WO 98 42741 A (GENETICS INST) 1 October 1998 (1998-10-01) page 68 -page 70	1-13, 21-26
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A	TASHIRO K. ET AL.: "SIGNAL SEQUENCE TRAP: A CLONING STRATEGY FOR SECRETED PROTEINS AND TYPE I MEMBRANE PROTEINS" SCIENCE, vol. 261, 1993, pages 600-603, XP002911163 ISSN: 0036-8075 the whole document	1-26
A .	WALLIN ET AL.: "Properties of N-terminal tails in G-protein coupled receptors: a statistical study" PROTEIN ENGINEERING, vol. 8, no. 7, pages 693-698, XP002102961 ISSN: 0269-2139 the whole document	1-26
A	EP 0 607 054 A (HONJO TASUKU ;0NO PHARMACEUTICAL CO (JP)) 20 July 1994 (1994-07-20) the whole document	1-26
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INTERNATIONAL SEARCH REPORT

ernational application No.

PCT/US 99/12252

Box !	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)	_
This Inte	emational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:	
2. X	Claims Nos.: 1,5-11 all incompl. because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically see FURTHER INFORMATION sheet PCT/ISA/210	
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)	٦
This Inte	mational Searching Authority found multiple inventions in this international application, as follows:	7
se	e additional sheet	
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.	
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.	
3	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:	
'	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos invention 1. claims 1-26 (all partially)	
Remark o	The additional search fees were accompanied by the applicant's protest No protest accompanied the payment of additional search fees.	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 1.2

Claims Nos.: 1,5-11 (all incompletely)

Claims 1 and 5-11 relate to polynucleotides defined as having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from a group of polypeptides listed in claim 1 (SEQ.IDs. 2, 6, 8, 14, 20). Back-translation of the polypeptide into DNA generates a very great number of nucleic acid sequences. It is not possible to search an entire database with this enormous set of sequences. The search thus has been limited to nucleic acid sequences having at least 80% homology with the nucleotide sequences as listed in claim 2 (SEQ.IDs. 1, 5, 7, 13, 19)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

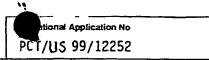
1. Claims: Invention 1: Claims 1-26 (all partially)

A membrane-bound protein as represented by SEQ.ID.2 and variants having 80% amino acid sequence identity therewith, a nucleic acid encoding said protein as represented by SEQ.ID.1 and variants having 80% nucleotide sequence identity therewith; a vector comprising said nucleic acid; a host cell comprising said vector; a process for the production of said protein; a chimeric molecule comprising said protein; an antibody specific for said protein; an extracellular domain of said protein; and a variant of said protein lacking its signal sequence.

2. Claims: Inventions 2-135: Claims 1-26 (all partially)

Idem as subject 1 but limited to one DNA sequence selected from SEQ.IDs. 1-424 and the corresponding polypeptide, wherein invention 2 is limited to SEQ.IDs. 5 and 6, invention 3 is limited to SEQ.IDs. 7 and 8, invention 4 is limited to SEQ.IDs. 13 and 14 and invention 135 is limited to SEQ.IDs. 423 and 424.





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